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DIPHTHERIA AND ANTITOXIN

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BY

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PREFACE

THIS little book had its origin in sundry papers read before meetings of the British Medical Association in recent years. The complications and sequelæ were originally dealt with at Maidstone. The results of some of the earlier cases of treatment with antitoxin at the Evelina Hospital were detailed before the Clinical Society, and subsequently the notes of the cases appeared in the *Lancet* in January 1895.

The time seems now to have arrived when it may be useful to summarise the results of the antitoxin treatment. Free use has therefore been made of the Reports of the Medical Superintendents of the Metropolitan Asylums Board, and of the Report to the American Pediatric Society, which confirm in the most conclusive way my own observations. Though statistics have been quoted from these Reports, which deal with large numbers, the cases detailed in the following pages are all selected from those which have been under my care.

Antitoxin seems to have robbed diphtheria of most of its terror, and my experience, both in hospital work and in private practice, is that if used sufficiently early and sufficiently boldly, there is prospect of still further reduction in the mortality.

I have to acknowledge my indebtedness to Dr. CLIFFORD ALLBUTT's 'System of Medicine' for many facts connected with the spread of diphtheria.

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DIPHTHERIA AND ANTITOXIN

CHAPTER I

INTRODUCTORY—THE CAUSATION AND SPREAD OF DIPHTHERIA

Definition.—Diphtheria belongs to the class of acute infectious diseases caused by the development and the growth of a specific bacillary organism. The bacillus of diphtheria has been isolated and can be easily recognised, though certain bacilli exist which resemble the bacillus of diphtheria in many particulars, both in their outward appearance and in the symptoms which they appear to induce in the human body.

It may be useful to quote here four propositions which Dr. Thorne Thorne considers to be conclusively demonstrated respecting diphtheria: (1) Diphtheria is a specific infectious disease, primarily and preferentially affecting mucous surfaces, notably the upper portion of the respiratory and alimentary mucous tracts; also, but more rarely, affecting abraded surfaces of the skin. (2) Diphtheria appears first as a local disease, the part attacked being the seat of an inflammatory process characterised by the formation of a false membranous deposit. The system as a whole is secondarily affected, the general disease being a consequence of the local one. (3) Local diphtheria results from the reception at a particular point of the mucous membrane, and the subsequent development there, of a definite micro-organism, the *Klebs-Loeffler bacillus diphtheriæ.* This micro-organism, which is vegetable rather than animal in its nature, must therefore be regarded as the particulate and essential cause of the local disease. The general symptoms of diphtheria, on the other hand, are largely due to the absorption into the system of a chemical poison or toxin, a result of the life processes of the bacillus. (4) Diphtheria, or a disease *ejusdem generis*, is found in certain of the lower animals, and can be communicated to them from the human subject.

Origin and early history.—Though the bacillary origin of diphtheria has only been recognised in recent years since the growth of scientific research in that direction, yet the disease itself seems to have been known at a very early date. The old Arabian physicians prescribed many nostrums for a disorder of the throat which, from their accounts, may have been diphtheria, and since their time occasional references of a somewhat uncertain character are to be found in the medical literature of early times. We find, for instance, that the operation of laryngotomy was recommended in the first century B.C., and in the sixth century A.D. a certain physician refers to the existence of a false membrane in the throat and to the danger of detaching it. Much uncertainty about the true nature of the disease prevailed, however, until 1821, when Bretonneau disentangled true diphtheria from the many throat affections so closely resembling that disease, and employed the terms 'diphtheritis' and 'diphtheria.' One of the great difficulties in diagnosing diphtheria lies in the fact that it appears to be possible that a membrane may be produced by other micrococci as well as by the bacillus of Klebs and Loeffler.

Predisposing causes.—Diphtheria rarely, if ever, originates *de novo*. It seems to require some pre-existing disease upon which to graft itself, some predisposing causes which will foster its development, some medium peculiarly adapted for the growth of its own particular bacillus. These predisposing causes evidently exist more commonly in children than in adults, as by far the greater number of cases occur at an early age. At one time it was thought that both sexes shared the risk to this disease equally, but the elaborate statistics of Dr. W. R. Smith, Medical Officer of the London School Board, seem to prove that after the age of three female children become markedly and progressively more liable to attacks than male children, although before that age the numbers affected appear to be nearly equal as regards both sexes. Dr. W. R. Smith believes that this peculiarity is largely due to the different habits of the two sexes at the later ages. On the other hand, the results published by Henoch indicate that in his experience girls and boys are equally affected. The reason of this apparent disagreement may lie in the fact of the great similarity of habits of boys and girls of school age in Germany, while in England boys are allowed greater freedom from restraint.

With regard to age, there can be no doubt that the disease is essentially a disease of early childhood rather than of infancy. In his classification of cases which came under his observation, Henoch found that

108 occurred during the first year
542 from the age of 1 to 6
107 ,, ,, 7 ,, 8
96 ,, ,, 8 ,, 14

Dr. Smith's statistics are based upon a larger number of cases, and they confirm these results. According to Dr. Smith, infants under one year are remarkably exempt, and the liability to the disease increases steadily in children from that age up to four years, after which it gradually declines.

Geographical distribution.—Like other infectious diseases this disease appears to travel—that is, to change its geographical locality from time to time, the cases occurring in groups in the areas affected.

In England diphtheria has been more or less continuously present since 1855. For the last twenty years the mortality from diphtheria has in this country increased rapidly, and this increase has been more marked during the recent years of that period. During the forty years that diphtheria has been present in England there has been considerable change in the affected areas. At one time the disease was especially rife in the crowded population of the Midlands and the North, but it seems now to have deserted these districts and to have been gradually drawn towards the south-east corner of England, and to have formed a centre for itself in and round London; indeed, during the last five years it appears to have been almost confined to the Home Counties, together with Sussex and Suffolk. At the same time, as Dr. Smith ingeniously points out, other infectious diseases, like scarlet fever and measles, have not shown the same variation of geographical distribution during the same period. These facts seem to indicate that in the affected centres some special local condition has influenced in a curious way the growth and development of diphtheria. Areas which favour the retention of damp or of decaying organic matter in the soil, areas also that are exposed to cold wet winds, seem to foster diphtheria.

Season.—Diphtheria occurs at all times of the year, but Henoch has pointed out that though Berlin is never free from diphtheria, allowance must be made for special increases at special seasons. Other observers have recently published results showing that during the second quarter of the year the smallest number of fatal attacks are registered, while the rate of mortality is at its highest during the fourth quarter. Dr. Thorne Thorne has recently shown that the increase of mortality at the beginning of the fourth quarter results from the large number of attacks in September, and that many of the deaths registered in the first quarter of the year are due to attacks commencing in the later part of the fourth quarter. Thus it seems conclusively to be shown that October and November constitute the season of normal extra-activity of diphtheria. This phenomenon has been explained in various ways by different writers. Some speak of the re-opening of the schools after the summer vacation, others of the abnormal activity of germs in the autumn, others of the change of weather from the bright sunshine of summer to the mist and cold of autumn, which by producing catarrhs of the respiratory passages prepare a fertile ground for the diphtheritic bacillus to develop.

However this may be, it is probable that various causes tend to affect children in a deleterious manner at that time of the year, and to render them more liable to diphtheritic attacks. As regards school influence, Dr. Thorne Thorne has summarised the methods in which it appears to him to be operative in the spread of diphtheria: (1) 'It brings together those members of the community who are by reason of age most susceptible to diphtheria. (2) The children thus brought together are placed and remain for many hours of the day in exceptionally close relation to each other. (3) The closer the aggregation and the greater the hindrance to free movement of air, the greater the risk. (4) The faulty sanitary circumstances in the school-house and its surroundings, and such other conditions as tend to general ill-health, in so far as they induce sore throat, favour the reception of any imported diphtheria infection. (5) There are ample grounds for believing that the aggregation of children in elementary schools constitutes one of the conditions under which a form of disease of particular potency for spread and for death may be manufactured. (6) The practices of kissing and of transferring sweetmeats from mouth to mouth, practices more common among girls than boys, the joint use of drinking cups and the like, must assist in the diffusion of diphtheria amongst schoolfellows.'

The spread of diphtheria is certainly often due to direct infection from one person to another, and schoolfellows run considerable risk during an epidemic of diphtheria, as those suffering from a mild type of the disease may communicate it to others, before it has been recognised as diphtheria; in the same way nurses, relations and friends of those affected may, unless great care is taken, contract the disease. . Another cause of the spread of diphtheria is through insufficient disinfection of the house, clothing, or bedding of the patient. In a damp house, it appears that the bacillus of diphtheria retains its vitality far longer than in a dry house. It is also a fact that can no longer be doubted that diphtheria may be carried by the bedding and clothing of patients. Instances of the spread of the disease in this manner are too numerous to be ignored.

Milk that has been contaminated may also prove an important agent in the spread of the disease. In 1878 many outbreaks were traced by Mr. W. H. Power to the distribution of a contaminated milk supply. There are several ways in which milk may thus become dangerous. (1) From infection with diphtheria poison from those who are engaged in the farm or milk shop; however mild the form of diphtheria may be from which they suffer, it can infect the milk, and, once infected, milk is a good medium for the development of the bacillus, which will thus be carried to all the customers of that dairy. (2) Milk may be infected with the diphtheria poison from a disease in the cows themselves. Cows which have recently calved frequently suffer from an infectious eruption called by farmers 'chapped teats.' A similar disease can be produced in cows by inoculation with the diphtheria bacillus, and the milk from these cows contains the diphtheria bacillus in abundance. Stored milk is more dangerous than fresh milk. For instance, in the milk which has been set for cream the diphtheria bacillus has been found in greater quantity than in fresh milk from the same source, the organism having had more time to develop in the former case.

Another source of infection may be provided by the pet animals of the household. Cats have been frequently known to suffer from an infectious disease resembling diphtheria, and in some cases this disease seems to have been given to the cat by the human subject, to have spread from cat to cat, and finally to have been transferred to human subjects again from the cat. This being the case, it is always well carefully to watch the health of the cats of a household during an outbreak of diphtheria.

Though the vast majority of the cases of diphtheria are certainly due to the causes of infection that have been enumerated above, it would be wrong to ignore the dangers that arise from faulty sanitation. Dr. Thorne Thorne says that the specific bacillus of diphtheria has never to his knowledge been discovered in sewer gas; at the same time there are a certain number of cases, consisting chiefly of single attacks in individual households, which do not seem to have become infected from pre-existing disease, and for which no explanation is forthcoming, unless it may be concluded that in rare instances diphtheria may be induced by faulty sanitary surroundings. Therefore, though the great increase of diphtheria in this country is certainly not due to bad drainage, yet it seems probable that a household sore throat may be induced by drain emanations, and that this sore throat may be most favourable to the reception and growth of the diphtheria bacillus, so that the minor affection may lead up to the major and more specific disease. Dr. Thorne Thorne considers that the increased occurrence of diphtheria is principally due to school influence and the agency of milk, and that these two sources of infection should be carefully watched and studied in order that the means of prevention may be more effectually carried out.

The prophylaxis or prevention of diphtheria has occupied the attention of many of the medical officers of health in all parts of the country. It is easy to lay down certain broad rules that may be followed with advantage. Families with a tendency to suffer from sore throat should avoid residing in places subject to cold wet winds, or on soil that retains damp and organic *débris*. Faulty sanitary conditions which may induce sore throat should be promptly remedied; milk should be scalded, for it is an established fact that milk that has been exposed for five minutes to a temperature of 60° Centigrade (140° Fahrenheit) is free from the diphtheria bacillus, or, at any rate, the vitality of the bacillus is thus destroyed. Any domestic animals, and especially cats, if they are in bad health should be carefully kept from association with the children. Infected persons should be most strictly isolated, and all the apartments and articles they have used thoroughly disinfected at the close of the illness.

With regard to boarding schools, if the disease continues to spread after the first few cases have been isolated, the school should at once be broken up and the whole place thoroughly disinfected. Day schools also should be closed for a time if, after the exclusion of all members of a family suffering from diphtheria, the disease spreads amongst the children attending the school. Again, if there is a fresh outbreak after re-opening, the school ought to be closed again, as evidently the specific bacillus still exists in the throats of some of the convalescents. It has been shown by cultivations that this bacillus may exist in a state of vitality for several weeks after the sore throat is apparently well. If the school be kept open during an outbreak of diphtheria, under no circumstances should a child be allowed to return to the school before at least two weeks have elapsed after the convalescence of every member of the family who has suffered from sore throat. Precautions should also be taken in the school to prevent the children using the same drinking cups or other articles; the children also should not be allowed to kiss each other.

CHAPTER II

SYMPTOMS OF DIPHTHERIA

Symptoms.—After exposure to the poison of diphtheria, the incubation period of the disease has been estimated to vary from seven days in extreme cases to twelve hours in exceptional cases. Experimentally, however, the time of incubation has been usually found to fall within three days. When the infection has been acquired under ordinary circumstances, the throat in all probability shows its first indication of change in from one to four days from the time of infection. At the commencement of the disease it is very easy to overlook its serious character, as the mode of onset is often somewhat obscure. The early symptoms may be merely feelings of malaise, headache, loss of appetite, some nausea, pain in the back or limbs; and as these symptoms might very well be due to other causes, they are often disregarded or underrated, and thus valuable time may be lost. Amongst infants and very young children, however, the apparent onset of the disease is usually sudden and severe, the early stages, prior to urgent laryngeal symptoms, escaping observation.

It is only after these indeterminate symptoms that attention may be directed to the throat by certain slight sensations of discomfort. This discomfort does not at first usually cause actual pain during the act of swallowing, but consists more often of pain at the angle of the jaw. It is also noteworthy that though the patient may complain somewhat of stiffness during movements of the neck, there is usually no complaint of discomfort on opening the mouth. These symptoms are important, as they are of material aid in distinguishing between the symptoms of cases of diphtheria and those of the simpler forms of tonsillitis. It is quite exceptional to find the onset of the disease marked by more violent symptoms, though in rare cases rigors may occur, and occasionally other symptoms, such as vomiting and diarrhœa, precede the rise of temperature. Vomiting, however, does not often occur in connection with the early stages of diphtheria; it is far more frequently a premonitory symptom of scarlet fever. During the development of the local manifestations the temperature usually rises somewhat, the range generally being within 101° to 102°. The early course of diphtheria is generally marked by slight evening exacerbations. (Figs. 1 and 2.)

It is quite exceptional for the temperature in the early days to rise above 102°, and in fact this comparatively low range of temperature is one of the most helpful means of distinguishing between diphtheria and the more simple forms of affections of the tonsils. Indeed, it is quite possible for the temperature to remain normal from the commencement of the disease, which is marked rather by changes of temperament and of appetite. When a further rise of temperature occurs during the course of the disease, it is an indication as a rule that there is an extension of the area affected.

Large patch on tonsil; recovery.—Fred. T. A——, aged six years, was admitted on November 5, 1894, with diphtheria of five days' duration. He was a well-nourished boy with a good family history. There was slight congestion of the tonsils and soft palate, and on the right tonsil there was a large grey patch of membrane. The uvula was clean, but slightly œdematous, and there were enlarged glands in the submaxillary region. The pulse was good, full, and strong, and 96 per minute; the respiration was 32 and not impeded; and the temperature was 100·4° F.

There was no albumen in the urine. Two hours after admission 10 c.c. of Behring's antitoxin were injected into the muscles of the thigh. Three hours later the pulse was 108, the respiration 26, and the temperature 102°, the patient feeling very well. Six hours later the membrane had become almost detached, the patient still feeling very well. Next morningthe pulse was 100, the respiration 24, and the temperature 98°. The patient took a hearty meal and did not complain of any pain in the throat. There was no albumen in the urine, and the throat had completely cleared. The patient was discharged on the sixth day practically well.

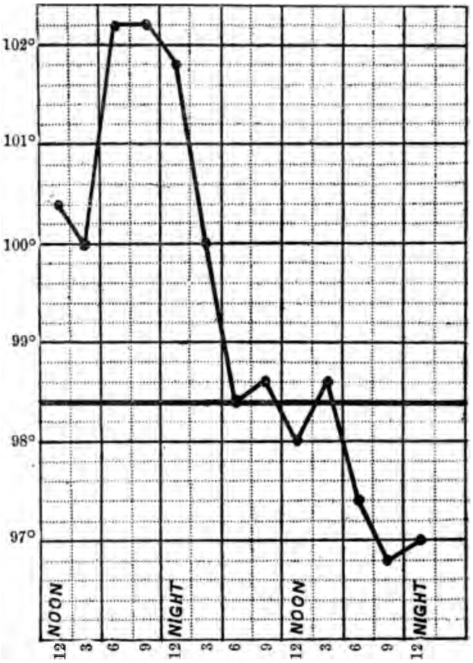

FIG. 1.—F. T. A., AGED 6 YEARS. ADMITTED NOVEMBER 5, 1894. ANTITOXIN INJECTED AT 3 P.M. ON DAY OF ADMISSION.

The exceptional occurrence of high temperature with the onset of diphtheria may be illustrated by the following case and the accompanying chart. (See also charts on pp. 36 and 120.)

Tonsil and uvula ; recovery.—Thos. D. M——, aged three years and nine months, was admitted on December 10, 1894, with sore throat of five days' duration, which was rapidly getting worse. The throat was congested, the uvula œdematous, and there was a patch of whitish membrane on the left tonsil. There was a faint trace of albumen in the urine. The temperature was 104° F., the respiration 28, and the pulse good (134). On the patient's admission 10 c.c. of Behring's No. 1 solution were injected, and six hours later the pulse was 120, the respiration 18, and the temperature 98°. Next morning the throat was quite clean and the general condition excellent. Since then there has been uninterrupted recovery. (Fig. 3.)

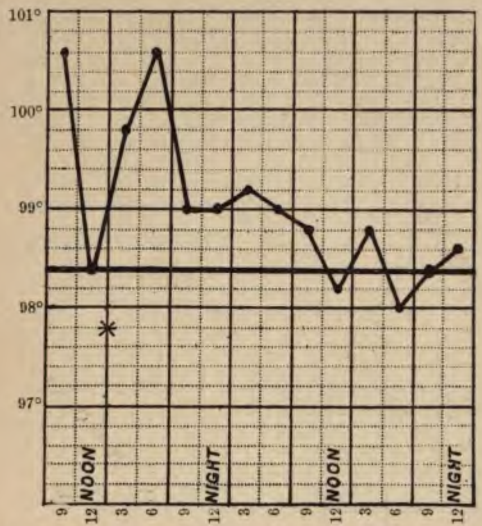

FIG. 2.—J. B., AGED 5 YEARS. ADMITTED JANUARY 26, 1895.
ANTITOXIN INJECTED AT 1 P.M.

Pulse.—The pulse is most helpful in the diagnosis of diphtheria ; its chief characteristic is its disproportionate rapidity as compared with the temperature. The pulse in diphtheria is commonly far more frequent than it is in cases of sore throat, as in tonsillitis or scarlet fever, which are marked by much higher temperatures. During the course of the disease, however, this disproportionate rapidity may be subject to considerable variations; these variations may occur within a few hours, and may often be accompanied by alterations of force and regularity. Sometimes the pulse becomes abnormally slow, a change which usually indicates the development of some complication. The variations of the pulse must be carefully watched, as they often afford useful warnings in cases which otherwise appear to be progressing favourably.

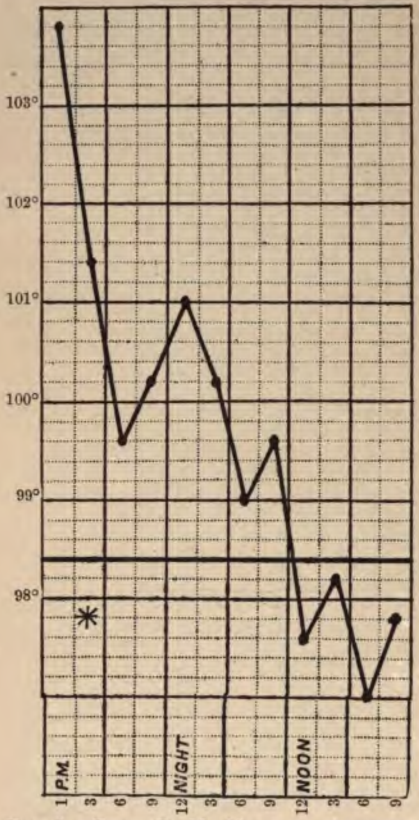

FIG. 3.—THOS. D. M., 3¾ YEARS. ADMITTED DECEMBER 10, 1894. ANTITOXIN INJECTED AT 2 P.M.

Malignant diphtheria with pulse changes.—Ellen M——, aged five years. Admitted December 8, 1893. Breathing very laboured on admission; pulse weak; very restless, wandering; cough frequent and troublesome; much discharge from the nose; face flushed. Slept very little during the night. Was given milk and brandy, but only swallowed a small portion with difficulty. Breathing continued very laboured; pulse at times imperceptible; face pale and blue; throat swollen and red outside; sick once; hands and feet cold. On the following day pulse imperceptible; breathing still very laboured; unable to swallow; much cyanosis;

slightly convulsed at 11 A.M. and died a few minutes after. In hospital only 24 hours. The temperature ranged from 100° to 101°, while the pulse varied between 128 and 152.

The further consideration of the alterations of the pulse may, however, be more appropriately dealt with amongst the symptoms marking convalescence.

Albuminuria.—In a very large proportion of cases of diphtheria, the urine, either at the commencement or at some stage of the disease, will be found to contain albumen. The amount present is not constant, it is subject to considerable daily variations, and generally there are no symptoms whatever indicating the existence of albuminuria. Most commonly the albumen is found only in very small quantity; frequently there is only sufficient to give a very faint haze on the addition of cold nitric acid. In rare cases, however, the amount may be very much larger, especially in cases where the disease is of a severe type. Mostly the existence of albumen does not afford any indication of the severity of the disease, and its presence or absence can scarcely be regarded as an indication of danger, or of improvement. In very severe cases the albumen sometimes becomes more persistent and larger in quantity. All that can be said of the importance of albuminuria in diphtheria is that when copious in quantity it accompanies other severe symptoms; it does not in itself appear to give rise to any distinct symptoms, and so far as my observation goes it does not leave any permanent trouble, although when death occurs in severe cases the kidneys are commonly found to be engorged. No permanent nephritic changes appear to result in cases that recover, and for those that die, they die as a consequence of the severity of other symptoms, and not as a result of any symptoms referable to the albuminuria. In very rare cases one may find that a small quantity of blood is present in addition to the albumen, but most commonly the appearance of the urine is not altered in any way, and without careful testing from day to day, and almost from hour to hour, it would be impossible to say from other symptoms that albuminuria was present or absent. Occasionally complete suppression of urine occurs in some fatal cases, and in these vomiting and cardiac depression frequently form the prominent symptoms. These cases of suppression, however, must be carefully differentiated from those of albuminuria; they are in no sense the result of the albuminuria, and in no sense comparable to the diminution of urine which occurs in the course of scarlatinal nephritis. The alteration in the urine is also curious in not being associated with any symptoms of dropsy, of headache, or of vomiting, referable to the presence of albumen. According to some observers a condition termed diphtheritic nephritis sets in, commonly at the height of the diphtheria, at about the fourth day, and it is characterised not only by the presence of albumen, but by diminution of the quantity of urine passed. According to others, the frequency of albuminuria has, in later days, been much increased by the administration of antitoxin. It is noteworthy that Henoch, writing many years before the introduction of antitoxin, considered that albuminuria occurred in about half the cases of diphtheria, whereas in the returns from the Metropolitan Asylums Board, 1896, in the two years previous to the introduction of antitoxin, albuminuria occurred in 24·1 per cent. and 28·6 per cent. of the cases, while in the year 1895, during which antitoxin had been employed, albuminuric cases were only 41·5 per cent., still, therefore, falling below the percentage recognised by Henoch, in the fourth edition of his 'Lectures on Children's Diseases,' published in 1889. My own experience corresponds with that of Henoch, and I regard the albuminuria, as a rule, as merely one of the side phenomena of the disease. It is not worth anxiety, unless the albumen exceeds about 30 per cent. Even in severe cases, the albuminuria frequently disappears entirely without any modification of diet or treatment and returns later, long after the throat symptoms have subsided. In these cases it would appear almost as though the albuminuria was to be reckoned among the sequelæ, and further consideration of it will therefore be found on page 54. Although from its frequency in diphtheria it might almost be regarded as an aid to diagnosis, it unfortunately occurs in many other varieties of inflammatory throat affections which are non-diphtheritic, hence, as giving rise to no symptoms, as being an uncertain sign of diphtheria, and as a condition which is not always present, the importance of albuminuria in most cases appears to be very slight; it is only of serious import where it becomes an element of prognosis, and in severe cases the albuminuria is merely one amongst many indications of the severity of the attack, and is not in itself a complication from which danger is to be anticipated.

Casts and epithelial cells are sometimes to be found, especially when the albuminuria is great in amount. The casts vary considerably, both in size and in appearance, being hyaline, granular, and epithelial. In addition to true renal epithelial cells, numerous leucocytes are mostly seen. As in most other diseases associated with wasting and variations of temperature, even though moderate, frequently an excess of urea is to be found.

Amongst the early symptoms of importance in aiding the diagnosis must be noted the alteration in the colour of the skin. Quite at the beginning, especially in very young children, the skin exhibits an amount of pallor and waxiness which is almost suggestive of severe hæmorrhage. This is totally independent of any interference with the oxidation of the blood, and therefore is independent of any marked interference with respiration, or with any increase in the rapidity of respiration. The pallor affects not only the skin but also the mucous membranes, and is especially noteworthy on the lips. Of the precise changes which produce these alterations very little is known; microscopical examinations have led to no result.

Sometimes, in severe cases, there is a tendency to spontaneous hæmorrhages, either occurring in the skin or the mucous membranes, and leading occasionally to severe hæmorrhages not only from the nose but also from the throat. In one such case which occurred recently at the Evelina Hospital the hæmorrhage appeared to have come from ulceration of a branch of the tonsillar artery, and was so severe that death ensued within a few hours. In other cases that have come under my observation, epistaxis has been sufficient to cause much anxiety, and in these cases the hæmorrhage has mostly been associated with diphtheritic changes within the nasal passages. In a minor form hæmorrhage from the nose is fairly common in cases of nasal diphtheria, and in these leads to a sanious discharge from the nose. Very rarely hæmaturia occurs in connection with diphtheria, but hæmorrhages from the stomach and from the bowels have been met with. It is only in exceptional cases that the hæmorrhage is sufficiently severe to cause immediate death, but it is always to be feared, as it adds so largely to the pre-existing weakness.

The disease is essentially one in which the depression of the vital powers constitutes the chief source of danger, and any complication, like hæmorrhage, which tends further to weaken the patient, will therefore add considerably to the risks incurred. The chief weakness of diphtheria is always manifested through the circulatory system; failure of the heart's action, variations in the rapidity and the strength of the pulse always constitute signs of danger, and it is obvious that hæmorrhages, if large in amount, will add materially to the risks of cardiac failure. Amongst other forms of hæmorrhage that have been described in connection with diphtheria may be mentioned cerebral hæmorrhage, but no instance of this has come under my observation.

Vomiting.—Severe cases are sometimes complicated by vomiting. It has been asserted that sometimes this symptom is an indication of an extension of the disease to the œsophagus or to the stomach. It most commonly occurs when the urine has been suppressed, and in such cases it may be accompanied by convulsions shortly before the fatal termination. Mostly, however, vomiting merely contributes one more link to the chain of symptoms producing cardiac failure and fatal collapse. The symptom is one which must always create much anxiety, as it is so frequently the prelude to the fatal termination, and it so often defies all attempts at treatment.

Diarrhœa.—It is not uncommon to find the vomiting of severe cases associated with frequent and intractable diarrhœa. This symptom may occur for three or four days before the fatal termination, and it contributes largely to the profound asthenia characteristic of malignant cases.

As the local manifestations of the disease develop, the voice generally changes in character; in some cases the vocal tone may be lost, in others the voice may merely have a hoarse sound. At the same time there may be a great deal of cough, sometimes of an irritative nature, but the cough is more usually associated with stridor and dyspnœa, which may occasionally proceed to symptoms of great distress from true spasm of the glottis. The child may also complain of dryness in the throat, and even in mild cases there is as a rule an ineffectual tendency to remove mucus from the fauces. It is probable that at this stage the local manifestations may be recognised and diphtheria undoubtedly diagnosed, since this disease in the large majority of cases primarily affects the fauces. Sometimes the fauces and the larynx are affected almost simultaneously, and in some cases both the fauces and the nostrils at this stage show the customary appearances of diphtheria.

Having considered the symptoms which are common to all forms of diphtheria, I will now indicate the modifications which occur when the bacillus attacks particular sites. Although the disease, whatever may be the part affected, is generically the same and has certain broad characteristics, its importance and its symptoms are largely influenced by its anatomical distribution.

The symptoms of diphtheria are almost entirely dependent upon three factors:—(1) the part which is attacked, (2) the degree of obstruction to respiration, and (3) the amount of absorption of poison from the original site of infection. It is obvious with a disease which attacks sometimes a tonsil or a portion of the pharynx, and sometimes the larynx or the trachea, that the severity will depend, not so much upon the amount of membrane formed, as upon the site attacked. Cases of diphtheria have been classified from the clinical side, according to their frequency of occurrence, into (1) pharyngeal, (2) laryngeal, (3) nasal, (4) ocular, (5) cutaneous, and (6) aural. Of these the most serious are undoubtedly pharyngeal, laryngeal, and nasal. Pharyngeal has been sometimes described as 'diphtheritic sore throat;' while to laryngeal the term 'diphtheritic croup' has been assigned.

As ocular, cutaneous, and aural diphtheria are relatively rare, and usually produce no serious constitutional symptoms apart from those common to the more severe forms of diphtheria, they may be dismissed from further consideration. Nasal diphtheria is so frequently of severe type that it will be dealt with under the heading of 'malignant diphtheria.'

Pharyngeal diphtheria.—This is the commonest variety, though the extent to which the membrane develops upon the pharynx and the severity of the symptoms are subject to considerable variations.

The tonsil and fauces when first affected are found to be red, swollen and œdematous, and shortly after these changes are observed the characteristic patches appear. The patch is usually at first of a bluish-white, semi-transparent nature, but if observed a few hours after its formation, it will be found to be white or yellow and opaque. The patches increase in thickness within a very few hours of their formation, and gain the characteristic 'wash-leather' appearance, though later they may become greyish and gangrenous. The edges of the patches are frequently everted, indicating a tendency to spontaneous separation. They often extend rapidly and may detach readily, leaving a raw ulcerated surface, which sometimes exudes blood, especially if the membrane has been forcibly separated. After the separation the patches quickly re-form and frequently spread to the uvula, and in many cases to the soft palate. Sometimes both sides of the fauces are affected in turn. The posterior surface of the soft palate appears frequently to be covered with membrane, even when only a small quantity of membrane may be seen at the tip of the uvula. If the uvula is drawn forward slightly, the posterior surface is usually found to be completely covered. In these cases the membrane undoubtedly affects the nasal passages, and there is often considerable nasal discharge. This discharge is offensive and irritating; it is sometimes, but not always, tinged with blood, and it frequently causes soreness of the upper lip. In some few cases of diphtheria the course is marked by sudden and severe epistaxis, and this symptom must be regarded as of considerable importance, for it indicates an extension of the disease beyond parts that can be seen. In true diphtheria the cervical glands at the angle of the jaw are mostly enlarged and tender, and this enlargement, as has before been noted, may serve to direct attention to the true nature of the disease. In some cases the whole chain of the cervical glands may be involved, but more usually there appears to be a single large mass of glands at the angle of the jaw inseparable from the parotid. Generally this enlargement shows no tendency to suppuration, but occasionally, especially in severe and malignant cases, the skin over the glands becomes red and œdematous, and signs of suppuration develop and require special treatment.

In its simplest form, when attacking one tonsil only, in the early stages the symptoms resemble closely those of so-called follicular tonsillitis, but cases of diphtheria may be distinguished by the pain on swallowing being relatively insignificant, by the comparatively low temperature in the early stages, and by the rapidity of the pulse which throughout the disease is generally out of all proportion to the temperature. Although these differences hold good for a large number of cases, it must be admitted that frequently considerable difficulty is felt about the diagnosis. Sometimes the nature of the case is rendered evident by the subsequent course; sometimes, in mild cases, the tonsillar affection improves so rapidly that, unless bacteriological investigations are made, an accurate diagnosis is almost impossible. All practitioners must have met with cases in which diphtheritic sequelæ, occurring a month or six weeks later, have been the first certain indications of the nature of the disease. In hospital work patients are frequently brought with diphtheritic sequelæ where the initial diphtheritic attack has been so slight as to have almost escaped observation.

One symptom which affords a certain amount of help in diagnosis of any form of diphtheria is the early abolition of the knee jerk. This occurs in a large number of cases, and unless the condition of the child is very urgent, the symptom is one which should always be sought for. It is well to remember that it is not necessary to lift a child out of bed to determine the presence or absence of knee jerk. It may frequently be recognised by placing the hand over the rectus femoris while the ligamentum patella is lightly struck. Contractile movement of the muscles may then be felt under the hand, even though the foot is not visibly moved. The value of this symptom for diagnostic purposes is very great, and it is so easily recognised, and it differentiates so thoroughly from ordinary tonsillitis, that it should not be neglected.

As a rule it is only in slight cases of pharyngeal diphtheria that much uncertainty about the diagnosis arises. When the membrane spreads so as to cover the tonsil completely, and when it re-forms quickly after it has been accidentally or intentionally detached, there can be little doubt about the nature of the case. Sometimes commencing on one tonsil, the diphtheritic patches extend speedily to the soft palate, to the uvula and to the pharynx. Occasionally the tonsil on the opposite side may in turn be affected, but in these cases the clinical diagnosis is usually sufficiently certain.

In the course of any form of diphtheria a rash may sometimes appear. This rash frequently resembles that of scarlet fever, but sometimes the characters are like those of measles, roseola or urticaria. Except in so far as the rash may cause some uncertainty about the diagnosis, it appears to have no importance. It is rarely followed by desquamation, and it is rarely accompanied by any alteration of temperature.

In very severe forms of pharyngeal diphtheria, the diphtheritic patches not only extend over wide areas but may lead to considerable destruction of tissue. Commonly the patch deepens in colour and increases in thickness during successive days, becoming brown or hæmorrhagic, while the surrounding portions of the pharynx or tonsils appear deep red or purplish. In these cases the edge of the patch is always sharply differentiated from the surrounding tissue, and if the patch is removed a deep ulcer is commonly seen. When extending over the soft palate the ulcerative process may destroy one of the palatine arches or the whole of the uvula. This permanent destruction of tissue rarely affects the tonsils or the pharynx.

Delirium is a symptom which is occasionally met with in severe cases, but rarely in mild, and the delirium is usually of a quiet type.

Amongst symptoms of rare occurrence may be mentioned rheumatoid pains in the joints, which have been met with in some epidemics.

Although it is common to speak of pharyngeal diphtheria as distinguished from laryngeal, it is by no means unusual for the disease to extend from the pharynx to the larynx, when the clinical picture becomes totally changed. In most slight cases of pharyngeal diphtheria the symptoms depending upon the local infection predominate, but when the area involved is increased, general toxic symptoms divert attention from the local changes. These symptoms are due to the development and absorption of a distinct poison, which results from the growth of the bacillus. The chief of the toxic symptoms are the alterations in the character of the heart's action, the rapidity of the pulse, and the general depression of the nervous system. Whereas in mild cases the child may remain cheerful and bright almost throughout the disease, or may show some slight lassitude during the first rise of temperature, in severe cases the lassitude and depression, the anorexia and restlessness, serve to indicate sufficiently clearly the existence of a serious malady.

Laryngeal diphtheria.—Laryngeal diphtheria is by its symptoms so different from pharyngeal diphtheria that it deserves separate consideration. It may be either primary or secondary. In exceptional cases the larynx and trachea are affected without any indication of disease of the pharynx; more usually it is the result of an extension of the disease either from the nose or from the pharynx. The supervention of laryngeal diphtheria is marked by alterations affecting the voice and also affecting the mode of respiration. The voice usually is husky, weak, and hoarse; sometimes it may be almost or quite inaudible. The term *dysphonia* has been applied to these vocal alterations, the term *paraphonia* has been used to include cases where the voice is merely hoarse, or even metallic, while *aphonia* indicates the total suppression of true laryngeal sound, the speech in this case being reduced to whispering sounds devoid of any true laryngeal note. With these alterations of voice, cough is also frequent, and the cough may be harsh, dry, shrill, or hoarse. The croupy cough of laryngeal diphtheria is, however, difficult to describe in words, but it has qualities which are not likely to be overlooked or mistaken by any one having experience of previous cases. The changes in the voice and the changes in the cough are, as Trousseau has pointed out, dependent upon the formation of membrane on the lips of the glottis, and the voice and the cough will become modified as the membrane increases in amount. Frequently after a period of complete aphonia the hoarse cough and metallic voice may return, the membrane which had caused the aphonia having been detached and expectorated during violent expiratory efforts. In such cases this sign of improvement is not usually permanent; the voice and cough may later again lose their tonic qualities.

Interference with respiration is an early symptom in cases of laryngeal diphtheria, and is marked partly by stridor and partly by dyspnœa. The stridor originates within the larynx, and may be so great as to mask the ordinary vesicular murmurs on auscultation over the chest. Commonly, of the two movements of respiration, inspiration is the one most affected. The act of inspiration is prolonged considerably, and is accompanied by indications of laryngeal obstruction, shown chiefly by the employment of the muscles of forced inspiration. In severe cases the obstruction leads not only to the employment of these muscles, but also to modification in the movements of the thorax. In rickety children, especially, these movements are accompanied by sucking-in of the lower costal margin with each inspiration; the forcible contraction of the diaphragm against the obstruction in the larynx leads to a recession of the lower costal margin with each diaphragmatic contraction.

A further indication of the obstruction to the entrance of air to the pharynx is seen in the spasmodic movements of the alæ nasi, which resemble closely those so often seen in cases of pneumonia occurring in children. Sometimes the alæ nasi are merely dilated during the act of inspiration, sometimes they are depressed during the act of expiration. The urgent need of air is also evidenced by violent up and down movements of the larynx during respiration, in fact the whole of the symptoms in severe cases point to abnormally violent muscular movements calculated to overcome laryngeal obstruction. Sometimes the movements of the larynx are so energetic that the heart's contractions are weakened during inspiration, a condition which can be recognised by alternating failure of the radial pulse.

Attacks of dyspnœa are frequently of varying intensity; the early attacks supervene after coughing, and the distress of breathing is always more marked during the night than during the day. Occasionally suffocative fits will come on suddenly, without any apparent exciting cause, and they lead to considerable distress, the restlessness, and the movements of the head, mouth, and of the muscles of the limbs indicating the sense of impending suffocation. These fits may last for four or five minutes and may be succeeded by a period of relative ease. Trousseau attributes them to spasmodic closure of the glottis caused either by the inflammation of the mucous membrane of the air passage, or by the presence of lymph poured out into its cavity. It is probably dependent upon a combination of both of these causes. The suffocative fits in severe cases become more frequent, the laryngeal sound may become permanent, and the features indicate not only deficient aeration, but also the sense of imminent danger.

The intermittent character of these suffocative attacks is extremely important, as it serves to distinguish cases of laryngeal dyspnœa from cases of dyspnœa due to interference with the functions of respiration, and the intermittence is in all probability due not so much to the presence of membrane as to the existence of spasm of the glottis. At the same time it is noteworthy that the membrane may be detached during the acts of vomiting or cough, and that any removal of membrane is likely to be succeeded by a period of quiescence. When strips of false membrane or casts from the trachea and bronchi have been expelled in this way, it is not uncommon for the child to sleep quietly for many hours. This period of relative comfort is apt to give rise to false hopes of permanent improvement, but the readiness with which the membrane re-forms must be remembered, and should serve to prevent any too hasty expressions of comfort. In some epidemics the tracheal or bronchial membrane seems to be expelled with extreme readiness. Trousseau has seen three or four successive false membranes expelled, and notwithstanding the relief afforded at each expulsion, has noticed the frequent fatal termination of such cases. The ready detachment of membrane, therefore, cannot serve as an indication of the permanent improvement of the case. A fatal result is not always to be expected in such cases, and in my own experience some of the cases from which the most perfect casts of trachea and bronchi have been expectorated have ultimately recovered.

Another noteworthy feature about cases of laryngeal diphtheria is the relative absence of severe constitutional disturbance during the early stages. This is perhaps partly to be explained by the absence of lymphatic glands connected with the larynx ; partly, also, it may result from the scant supply of lymphatic vessels. Such lymphatic vessels as there are, are connected with the bronchial glands, so that it is by no means uncommon to find considerable enlargement of the bronchial glands after death from laryngeal diphtheria.

In most cases the rule is for the disease to spread from the pharynx to the larynx and the trachea, or, as it has been termed, a downward extension. In rare cases, however, it would appear that it may begin either in the trachea or even in the bronchi, and that it may ascend from these to the larynx. According to Trousseau, in nineteen out of twenty cases the pharynx forms the starting point of the malady, and this also is the experience of Bretonneau and Guersant, and it is possible that some of the cases of reversed infection may be explained by the earlier symptoms of the pharyngeal malady having been overlooked. When the pharynx alone is involved, beyond some engorgement of the glands and some slight or trivial pain during deglutition, it is quite easy for the case to escape observation, so that there may have been time for pharyngeal membrane to have formed, to have detached, and for all traces of the pharyngeal disease to have disappeared, even though the process was extending onwards to the larynx. When the larynx is becoming involved, however, the symptoms at once become more urgent, and the end may be painfully near. The occasional absence of cough has been by some attributed to inability to close the glottis, so that only ineffectual efforts to cough can be made, similar to those of a patient upon whom tracheotomy has been performed.

The extension of the disease below the larynx is extremely uncertain in frequency. According to Bretonneau and Hussenot, in two-thirds of the cases membranes did not extend below the trachea. It is by no means uncommon to find after death false membrane lining the trachea, and sometimes in exceptional cases it may extend to the ramifications of the bronchial tubes. Mostly, however, the ultimate cause of death is cardiac failure or respiratory obstruction, independent of extension of membrane through the finer bronchi. Mostly, as Trousseau points out, the cases upon which tracheotomy has been performed succeed better when the operation has preceded the expulsion of membranous casts of the trachea, because in such cases there is distinct evidence that the disease is extending onwards, that it has got a firm hold on the system, and the danger of toxic symptoms is therefore greater.

In severe cases there is always considerable danger of pulmonary complications. When the channels through which air reaches the air cells are materially diminished in calibre, there is a tendency for the bases of the lungs to become engorged, and this engorgement is frequently of a pneumonic type. The occurrence of lung complications is usually to be recognised mainly by alterations in the physical signs, although some increased frequency of respiration may frequently serve as a clue. The physical signs are those of dulness on percussion, dulness which may be relative or absolute. Lung complications may occur in any form of diphtheria; sometimes they may be the indications of danger in the later stages of pharyngeal diphtheria, and the lung trouble then is the expression of the depressant influences at work. They may also develop at any stage of laryngeal diphtheria, either from the obstruction to the freedom of the air passages, or in later stages as evidence of extreme asthenia. They are not uncommon even during the stage of convalescence; indeed one of the chief dangers of the paralytic affections that so commonly ensue after diphtheria consists in the interference with the freedom of movement of the muscles of respiration. When the diaphragm or the intercostal muscles are affected severely, there is always considerable risk of the development of lung complications, and the fatal termination in such cases is undoubtedly mostly the result of lung engorgement or pneumonia. On the other hand, they may ensue after paralysis affecting the palate, pharyngeal and laryngeal muscles, and in such cases the lung trouble mostly results from irritation produced by particles of food which have entered the air passages. Owing to the paralytic conditions, not only may food set up irritation within the air passages, but the resulting bronchial secretions will tend to accumulate owing to the difficulty of coughing, the lungs will be imperfectly expanded, and some portion of the lung will frequently undergo collapse.

Another form of lung trouble which sometimes occurs during diphtheria is interlobular emphysema of the lungs, which is produced by rupture of the air vesicles during violent efforts to cough. This emphysema has been described as extending occasionally to the cellular tissue of the neck, the shoulders and the chest, and it has sometimes been attributed to the operation of tracheotomy, but in such cases in all probability it has been produced before the operation, and is in no sense a consequence of the operation.

Many observers have dwelt on the importance of laryngoscopic examinations in cases of suspected diphtheria, and although such examination might afford very useful indications which would tend to clear up cases of doubt, the examination is one which cannot easily be performed when dealing with infants ; and it is safer in case of doubt to be guided by the general symptoms rather than to attempt laryngoscopic examinations which might excite severe spasm of the glottis. Sometimes the diagnosis can be cleared up by the expulsion of shreds of membrane in the act of coughing, but in such cases certainty can only be established as the result of bacteriological examination. Dr. Dillon Brown, in the article on diphtheria in Starr's 'American Textbook of Diseases of Children,' states that 'the only constant and reliable guide as to the presence and the amount of laryngeal obstruction is obtained by auscultation of the chest and listening to the respiratory sound. This gives an accurate idea as to the amount of air entering the lungs.' Auscultation of the chest, however, can scarcely serve to indicate the amount of air entering the lungs, as in all cases of laryngeal diphtheria the stridor which results from partial occlusion of the glottis completely masks the vesicular murmur of the lung. The amount of laryngeal obstruction can only be inferred from the dyspnœa and its consequences. Attention must be paid to the rapidity of breathing and to the signs of interference with respiration as shown by the lividity of the face and lips, and as shown by the amount of sucking-in of the lower costal margin. These will afford useful indications when stethoscopic examination might be misleading.

With regard to the time of occurrence of lung trouble, in severe cases it may occur early; commonly it occurs between the second and the fourth day in cases of ordinary laryngeal diphtheria. I have not burdened the text with illustrative cases of ordinary pharyngeal and laryngeal diphtheria, as they occur so frequently, and the main features have already been detailed.

Malignant diphtheria.—Cases of malignant diphtheria in which the prognosis is extremely bad are characteristic of certain epidemics. As with other diseases of an infectious type, different epidemics differ materially in their severity. Sometimes we find that pharyngeal cases predominate, and the tendency may be towards recovery; sometimes the epidemic is marked by the occurrence of a large number of laryngeal cases, when the prognosis becomes more uncertain; and occasionally epidemics arise in which we find that the tendency is towards malignancy, and, previous to the introduction of antitoxin, no treatment appeared to be of any avail.

In these cases of malignant diphtheria considerable glandular engorgement is always present, and the inflammation, instead of being limited to the lymphatic glands, extends to the cellular tissues in their neighbourhood, and the skin covering these inflamed parts frequently becomes red and œdematous, the redness often looking like that associated with erysipelas, and the amount of swelling being suggestive of deep-seated inflammation. In these cases the glandular swelling commences on one side, below the angle of the lower jaw, the side affected corresponding with the side of the pharynx which is affected by the diphtheritic membrane. Mostly the engorgement only attacks the opposite side of the neck as the diphtheritic membrane extends to the opposite side.

In these malignant cases the membrane forms rapidly and extends rapidly, so that within a few hours the fauces and the whole of the posterior wall of the pharynx may be red, œdematous, and covered with patches of white or yellowish-white membrane. The inflammatory changes may sometimes involve the auditory passage through the eustachian tube, and very frequently the disease extends over the posterior surface of the palate to the nasal chambers. The danger in such cases is extreme, and when the nasal passages become affected in this way the patients rarely recover, whether adults or children.

Malignant diphtheria of palate, fauces and nose; death.—A girl aged eight years was admitted on November 7, 1894, with diphtheria of two days' history. The tonsils were much enlarged and covered with membrane, as also were the soft palate and uvula. Great pain on swallowing, profuse sanious nasal discharge, and much swelling on both sides of the neck. The pulse was 140 and very feeble, the temperature was 100·4° F., and the respiration 36. Ten cubic centimetres of Behring's No. 2 antitoxin were injected. The urine contained one-twelfth of albumen. The pulse improved a little and fell to 120. The respiration was 28, and the temperature 98°, but the throat did not improve and the glands increased in size. On November 9, 10 c.c. of Behring's No. 1 serum were injected. The pulse remained about 120 to 130, but became more feeble, and the first sound could scarcely be heard at the apex. The nasal discharge increased, and though the temperature remained normal, the patient became very cold and the skin clammy. On the 10th she three times vomited a quantity of laminated clot, which appeared to have been lying in the œsophagus for some time and was of a greyish colour. On the afternoon of that day the patient gave a sudden convulsive start and died suddenly, a quantity of black coffee-ground material pouring from the mouth. (Fig. 4.)

Necropsy.—There was very deep ulceration of the tonsils, and the right tonsillar artery was found to be laid open at the base of an ulcer for a distance of one-twelfth of an inch. There was a good deal of blood in the stomach, and the tissues in the submaxillary region were full of extravasated blood.

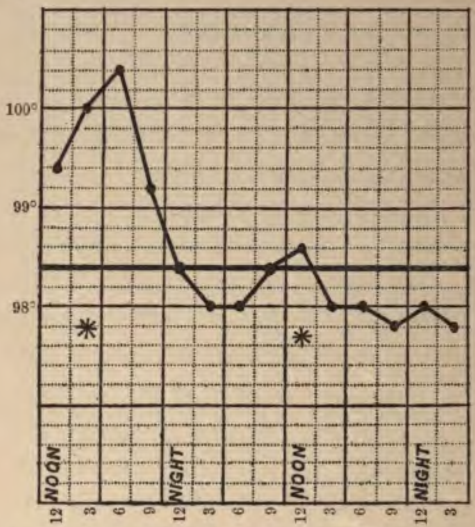

Fig. 4.—Vinny B., aged 8 years. Admitted November 7, 1894. Antitoxin injected at 2 p.m. on same day and at noon on the next day

The extension of the disease to the nasal passages may be inferred not only by sanious discharge from the nose and by fetid odour, but also by lachrymation, which is sometimes as severe as in persons suffering from obliteration of the nasal duct. This lachrymation is the direct consequence of obstruction of the nasal duct by inflammatory thickening of its lining membrane. In these cases it is not unusual to find that the conjunctiva shares the inflammatory changes, and is occasionally coated with false membrane.

John G. E——, aged one year and four months. Admitted at 5 p.m.; died at 2.30 a.m., so no previous history could be obtained. He was in a collapsed state when admitted, without any special difficulty in breathing; the pulse was very feeble and rapid; there was membrane on the fauces and on both the tonsils, and as there appeared to be no urgent need for tracheotomy it was not done. The nurse's notes are that on admission the pulse was very feeble, the extremities quite cold, frequent, short and hacking cough, especially after swallowing; breathing fairly easy; very slight sucking in at 7.30 P.M. Discharge from both eyes, more from the left. Slept for a few minutes, at intervals starting in sleep. Very restless and fretful when awake, and at times crying out as if in pain; face very pale, blue round the nose and mouth; slight sucking in at 8.30. Very thirsty and unconscious all night, groaning in sleep. At 2 A.M. pulse much weaker; nourishment returned through the nostrils; face very blue. Died at 2.30 A.M.

In malignant cases epistaxis is frequent, but bleeding may also occur from other mucous membranes. It is not uncommon for the disease to be complicated by hæmoptysis, by bleeding from the alimentary canal and bladder, and by subcutaneous hæmorrhages, thus much resembling the collection of symptoms found in hæmorrhagic small-pox, or in cases of poisoning by phosphorus. Another symptom which is extremely common in such cases and which adds greatly to the danger is the extreme distaste for food; the disease being one in which asthenia is the prominent symptom, any interference with the powers of nutrition will materially increase the risks. As the disease progresses towards its fatal termination, the surface becomes cold, and the patient may exhibit symptoms of extreme restlessness, tossing about and clutching at the bed-clothes or at the nurse, or the mother. Sometimes, however, in place of the restlessness, the child falls into a condition of torpor, and the end mostly occurs somewhat abruptly by the patient starting up in bed and then falling back in a fainting condition.

Malignant diphtheria.—Sarah K——, aged eight months. Admitted September 16, 1893. One brother was in a fever was considerable sanious discharge from the nose. Two hours after admission twenty minims of Aronson's antitoxin were injected into the subcutaneous tissue of the abdomen. Six hours later the pulse was 120, the respiration 36, and the temperature normal. The general condition was excellent. The next morning the pulse was 108, the respiration 24, and the temperature 97°; but there was still a slight patch on the tonsil, with soreness of the throat. After this the patient made a rapid recovery, and was discharged on the sixteenth day after admission practically cured. Besides the antitoxin treatment, a gargle of chlorine was used in this case. (Fig. 6.)

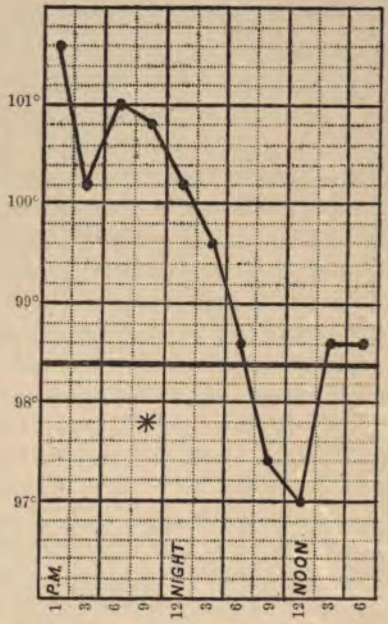

Fig. 6.—Henry V., aged 10 years. Admitted November 16, 1894. Antitoxin injected at 9.10 p.m.

Severe; naso-pharynx; recovery.—Frederick B——, aged six years, a well-nourished child, was admitted on December 5, 1894, suffering from a severe attack of diphtheria. The symptoms had been noticed for about three days. On admission the pulse was 140, small, weak, compressible, and very irregular; the respiration was 38, greatly embarrassed; and the temperature was 103° F. The throat was greatly swollen and the patient complained bitterly of pain on swallowing. There was a trace of albumen in the urine and a well-marked fetid discharge from the nasal cavity. On the right tonsil there was a complete layer of a whitish-grey membrane, which did not reach to the uvula or soft palate. On the left tonsil there was a smaller patch. The glands at the angle of the jaw were also enlarged. Soon after admission 5 c.c. of Behring's No. 1 solution were injected into the abdominal wall, but with slight effect, the pulse being 140, the respiration 34, the temperature remaining high, and the general symptoms increasing in severity. On the following day, the throat symptoms having become much worse, with great dyspnœa and marked signs of laryngeal obstruction, and the pulse also being very weak, compressible, and irregular, 10 c.c. of No. 2

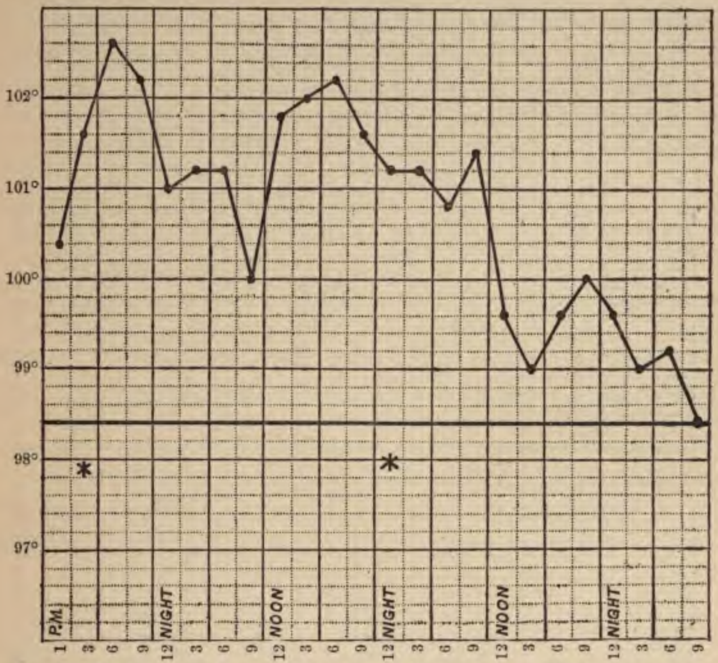

FIG. 7.—F. B., AGED 6 YEARS. ADMITTED DECEMBER 5, 1894. ANTITOXIN INJECTED TWICE *

Behring's solution were injected; this produced marked improvement, the pulse being reduced in four hours to 108 and becoming more regular, the respiration to 32 with less dyspnœa, and the temperature to 99·4°. The next morning the membrane on the throat, which had greatly spread, was nearly detached, the pulse being 120 and much stronger, and the respiration 32, easy and quiet. The child became quite convalescent and developed no bad symptoms. A chlorine gargle was used in this case, but antitoxin was the only medicine given. (Fig. 7.)

Soft palate, tonsil, naso-pharynx; tracheotomy; recovery.—Harold W——, aged five years, was admitted on December 19, 1894, and was said to have been ill for nine days. At the time of admission the child was very cold and cyanosed, with scarcely perceptible pulse and much dyspnœa. The pulse was 144, the respiration 36, and the temperature 97·6° F. The lower ribs were being sucked in violently. The soft palate, uvula and right tonsil were covered with membrane, and the cervical glands were much enlarged. Ten cubic centimetres of Behring's No. 3 antitoxin serum were injected at once. While taking a cultivation from the throat, the breathing became suddenly absolutely obstructed,

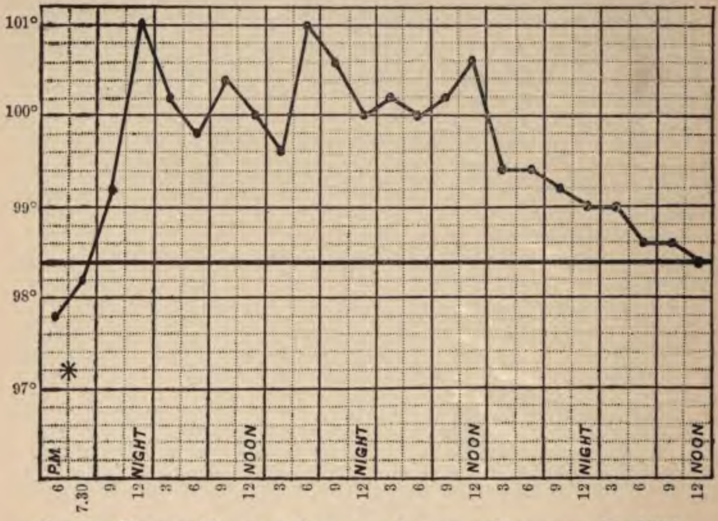

FIG. 8—HAROLD W., AGED 5 YEARS. ADMITTED DECEMBER 19, 1894. ANTITOXIN AT 6.30,* TRACHEOTOMY 6.45

and the child in a moment was flaccid and made no attempt at respiration. Tracheotomy was performed with a single incision, and after several minutes' artificial respiration some attempt at breathing became manifest, and in about fifteen minutes full respiration was restored. An hour later the pulse was 120, the respiration 28, and the colour good. The urine contained about one-thirtieth albumen, the heart dilated moderately, and the lungs were healthy. There was profuse discharge from the nose. The child slept well all night, the breathing being easy and quiet, with little coughing. In the morning the pulse was 144, being fairly good, the respiration 36, and the temperature rose to 101°. Food was well taken. The membrane had cleared off the tonsil, but remained on the uvula and edge of the soft palate. At 9 A.M. the pulse was 120, the respiration 26, and the temperature 100°. The colour was good. The child was well enough to play with toys and look at a picture book. At 9 P.M. the pulse was 124, and the respiration 28. The discharge from the nose had almost ceased. A good deal of tenacious mucus was being coughed up, but no membrane, and the throat looked less swollen and showed less membrane. The cervical glands were much less swollen. The child slept well. The heart sounds were good, and the patient was apparently quite comfortable. The cultivations showed Loeffler's bacillus and a few cocci. The child subsequently convalesced rapidly, with no bad symptoms. (Fig. 8.)

CHAPTER III

COMPLICATIONS AND SEQUELÆ OF DIPHTHERIA

Complications and sequelæ.—By far the most important of the complications and sequelæ of diphtheria are the various forms of diphtheritic paralysis. The time at which these occur is liable to considerable variation. As has before been mentioned, some paralysis of the tendon of the patella, tendon reflex, is frequently to be found quite early, and affords a valuable indication of the nature of the disease. Commonly paralytic symptoms appear at about the third or fourth week, and they then are to be regarded as sequels rather than as complications, inasmuch as they are separated from the original attack by a distinct interval, an interval during which convalescence has been apparently progressing satisfactorily. Paralytic symptoms, however, may occur as early as the fourth day of the disease, or they may be postponed until the tenth week from the commencement of the attack. No rule can be laid down for the occurrence of diphtheritic paralysis; it may appear after any form of diphtheria, whether slight or severe. Broadly speaking, it appears somewhat more common after the slighter cases of pharyngeal diphtheria, and it is by no means unusual to find that the true nature of the disease is only established with certainty by the subsequent occurrence of paralytic symptoms.

The laryngeal form is said to be less commonly associated with diphtheritic paralysis, though this relative immunity is possibly, as Dr. Gee remarks, owing to the fact that previous to the introduction of antitoxin few patients survived the primary disease; and it may be here noted that the relative increase of diphtheritic paralysis which has been stated to follow the antitoxin treatment may probably be explained by the decrease in the mortality produced by the antitoxin. As a larger number of patients survive, a larger number remain to be attacked by diphtheritic sequelæ. Of cases of pharyngeal diphtheria it has been estimated that at least one-tenth of the cases are affected later by some form of diphtheritic paralysis. It has been argued that the paralysis, being dependent upon the toxic influence of diphtheria, is therefore more likely to occur after slight cases than after those in which the poison exerts its main influence locally. During the primary attack, careful investigation will often reveal paralytic symptoms. The frequent abolition of the knee jerks formed the subject of a valuable paper by Dr. Hector Mackenzie (vol. xx., St. Thomas's Hospital Reports), and his observations are in close accordance with my own. In a large number of non-fatal cases the knee jerks disappear from the fourth to the tenth week, but in many of the fatal cases the knee jerks disappear more early, the percentage being greatest at the sixth day, although it is still high on the seventh and eighth day. The occurrence of this condition may be, and no doubt is, frequently overlooked in the more severe cases of diphtheria, since the urgency of the symptoms preclude all unnecessary disturbance of the patient. Still, even in the most urgent cases, the presence or absence of muscular contraction in the rectus femoris may with care be made out, even when the patient is lying on his back (see page 23).

Apart from this, perhaps the commonest form of paralysis is that which affects the soft palate, the laryngeal muscles and the muscles of deglutition. The paralysis seems to be due to true multiple peripheral neuritis, and in mild cases it will commonly last for a period of from two to six weeks, although in severe cases indications of paralysis may be found after several months, and paralytic symptoms following from diphtheria have been described as persisting for years. Broadly speaking, the paralytic symptoms are somewhat more frequent in adults than in children; but the possibility of error of observation must be here referred to, as in children it may be somewhat difficult to recognise milder forms of paralysis.

With regard to the paralysis of the soft palate, the laryngeal muscles and the muscles of deglutition, it is important to note that there is probably considerable impairment, or even total abolition, of sensation in addition to the loss of muscular contractility. The affection of the soft palate is usually indicated by regurgitation of fluids through the nose and by nasal twang of the voice. The velum palati in these cases is found to hang flaccid and to have lost all power of reflex contractility; the uvula commonly hangs down and points towards the affected side when the paralysis is unilateral. Sometimes the uvula appears as though glued to the arch of the palate and the tonsil. In mild cases deficient movement of the velum may be noted early, when the diphtheritic membrane has invaded the palate and the deficiency of movement may be observed, even though it is insufficient to affect deglutition to any obvious extent. When the paralysis of the palate is unilateral, the regurgitation of fluids usually occurs from one nostril, that of the affected side.

Diphtheritic paralysis without history of initial attack.—Ernest M——, aged seven years. Admitted July 15, 1889. No history of sore throat in patient or in any one in the neighbourhood. On July 13 the mother thought the child's nose was stuffed up, as he kept on 'snuffling' and talked very indistinctly.

On the evening of the 14th, whilst drinking water, some returned through the nose. On the day of admission he swallowed tea, while he had difficulty with bread and butter and 'choked' several times over it. No difficulty in breathing; seemed during sleep to breathe through the nose; speech had been getting indistinct, although usually a clear speaker. On admission, voice nasal; the left side of the palate seemed to have dropped and was a little lower than the right side; when swallowing fluids a little returned at times, and always through the left nostril. This child speedily recovered.

The diminished sensibility of the pharynx is frequently associated with diminished sensibility of the larynx. I have often noticed that distress of breathing and loose, rattling cough follow attempts to swallow liquids, and in such cases there can be little doubt that some fluid has passed into the air passages owing to the paralysis of sensation affecting the rima glottidis. It must not be inferred however that this is the explanation of all cases in which distress of breathing and even a fatal termination have followed shortly after fluids have been administered; more probably these result from implication of the pneumogastrics. When it is necessary to feed with the nasal tube, owing to the diminution of sensibility, there may be some danger of the tube being passed into the larynx and trachea, and of the bronchi being flooded, but even when a suspicion of this accident has been aroused, I have never been able to verify it upon the post-mortem table; indeed, such an accident is probably of very rare occurrence, as it must be rather a difficult thing to pass the nasal tube into the larynx. The tube always impinges first on the back of the pharynx, and then glides onwards along its posterior wall. Still, as there is a possibility of such an accident, it is well to make it a rule to wait a little while after introducing the nasal tube to see that the breathing, which is always momentarily checked, becomes thoroughly and easily re-established.

Paralysis of the laryngeal muscles sometimes gives rise to a good deal of trouble after tracheotomy. In one of my cases, after all urgent symptoms had passed off, every effort to remove the outer tracheotomy tube was followed by an arrest of respiration, and we had ultimately to intubate. In this case sensation was ultimately regained, and we were able to dispense with the tube. In a similar case there was reason to believe that the arrest of breathing resulted from sheer nervousness, as when one of my colleagues enlarged the tracheal opening and the larynx was viewed from below, the movements of the vocal cords were found to be under normal control.

Sometimes the tongue, the lips and the face exhibit indications of paralysis.

Facial paralysis is not very common as a sequel of diphtheria, but in 1893 I had a child under my care at the Evelina Hospital with this condition, and the diphtheritic origin, which was at first a matter of inference, was subsequently confirmed by affection of the palate, the extremities and the diaphragm. In the following case the paralysis of the face was unilateral and incomplete, resembling that seen in hemiplegia rather than the more complete form of Bell's paralysis.

Diphtheritic paralysis of face and palate.—Harry M——, aged five years. Admitted November 22, 1893. Six weeks previously had diphtheria; four weeks later had paralysis of left side of face, and fluids began to return through nose, and he lost power in his legs. On admission the soft palate was seen to be paralysed; he spoke with nasal voice. There was marked paralysis of facial muscles; orbital muscles were affected, but not to any marked extent, as the child was able to shut his eyes well. There was no squint; the knee jerks were absent. Three days after admission, paralysis of external rectus and inferior oblique of left eye noticed. On the 30th the diaphragm was found to be acting very slightly, and it was noticed that the pupils did not react to accommodation. By December 11 the muscles of the eye, diaphragm and palate had regained power, but the knee jerks were still absent.

Ocular paralysis is sometimes met with, and in such cases it is the muscles which fail rather than the sensory apparatus ; the vision may be indistinct and hazy, the power of accommodation being temporarily abolished. It is somewhat difficult to make sure when this condition occurs in young children, but it occurs relatively frequently in adults, and it is admirably described in Sir Thomas Watson's lectures by Sir William Priestley, who was himself the patient ; interference with the movements of the eye can be more readily noted, and the weakness and loss of power appear commonly to involve the external rectus, so that double vision results. In such cases the patient can commonly look forwards well enough, and the power of convergence is retained ; but when efforts are made to follow a moving body to one side of the head, a convergent squint is produced and causes double vision.

Diphtheritic paralysis affecting muscles of eyes, trunk and head.—Ada H——, aged four years. Admitted March 26, 1891. Diphtheria five weeks previously. Three weeks previously food came through her nose, and she talked through her nose. She became 'tottery' on her feet, and the day before admission she was unable to stand ; also unable to use her hands as well as before, seeming to get tired. Fairly healthy-looking ; internal strabismus affecting both eyes, more marked on the left side. Glands under jaw enlarged, speech indistinct, soft palate paralysed, with slight deviation of uvula to the left. Very unsteady on attempting to stand or walk, but could do both with difficulty ; very feeble hand-grasps on both sides ; no albumen ; pulse markedly weak ; anæsthesia of conjunctiva—finger could be passed all over conjunctiva without causing muscular contraction or pain ; pupils react to light and accommodation ; sight seems good. April 2, 1891: No food passing through nose; eyelids both droop; head either flexed or extended, falling backwards or forwards without muscular power to hold it in position; uvula central; slight movement of soft palate. On the 5th the child could not sit up, and complained of pain in the neck. On the 6th breathing became distressed, with restlessness and feeble pulse, and at 12 noon death ensued in spite of artificial respiration and a hypodermic injection of ether. In this child the temperature was generally subnormal, and the pulse varied from 80 to 132. The only abnormality found at the post-mortem examination was a rather tough white clot in the right ventricle.

Some slight deafness is sometimes met with in cases of diphtheria, but this is not so often a sequel as an accompaniment of the attack, and it is to be explained in the same way as the deafness of ordinary tonsillitis, or pharyngeal catarrh. In all probability, the intrinsic muscles of the ear are not involved in the majority of cases.

Of the other special senses it is extremely difficult, if not hopeless, to attempt to arrive at any conclusions in cases of children. Investigations of the senses of taste and smell present a hopeless task, since children so readily assent to any suggestion. A similar difficulty attends investigations concerning the sense of touch; a tingling numbness, pins and needles, and the sense of weight have, however, been referred to in descriptions of post-diphtheritic conditions affecting adults. An interesting case was recorded in the 'Lancet' (October 21, 1893), in which there was complete transference of sensation from one side of the body to the other. When any part—for example, the right hand—was touched, the sensation was immediately referred to the opposite side, a condition described under the term of 'allocheiria.' I have met with nothing like this in children, and I am afraid I should regard with some distrust a description of such symptoms coming from an adult.

Sometimes the muscles of the neck are involved in the diphtheritic paralysis, and the patient then becomes unable to control the movements or the position of the head.

Diphtheritic paralysis affecting palate, muscles of respiration, the muscles of extremities and of head.—Richard S——, aged three years. Admitted September 1, 1890. Two months previously feverish, cried when he coughed, getting poorly for three or four weeks. The last two days would not walk. Had discharge from nose streaked with blood. A month previously talked quite well, but on admission could scarcely be understood; cough suggestive of weakness of respiratory muscles; soft palate does not move on phonation; always able to drink unless a fit of coughing came on, when fluids passed through nose; patella reflexes absent. On the 5th it was noted that the head was not properly supported by the muscles of the neck, that it fell from before backwards, or *vice versâ* when the child's position was changed; frequent ineffectual cough. On the 8th paralysis of soft palate a little worse; held the head up better. The general condition improved, and on November 13 it was noted that the patella reflexes had returned; still some nasal twang. On December 18 the gait was still paralytic, and it was not until January 16, 1891, that the child was in a fit state to send to a convalescent home.

Of the extremities, the legs are commonly affected before the arms, and in many cases the muscles of the arms may completely escape. The paralysis of the legs is usually progressive. In its early stages it is indicated more by weakness than by actual loss of muscular contractility. The patient may be unable to stand steadily, or the gait may be somewhat staggering, while later, all power of motion may be lost, so that the patient is wholly unable to stand or even to raise his legs in the bed. Diphtheritic paralysis affecting the legs is usually somewhat tedious in its progress, and the volume of the muscles may be considerably diminished during the time of inactivity. The reactions of the muscles to faradisation are greatly reduced, or even totally lost, while the electrical reactions of the nerve trunks remain normal. Electrical reactions are however subject to considerable variations. Sometimes faradic excitability may still be diminished, while the voluntary motor power is being regained. Unlike the paralytic affections of the pharynx and larynx, we find that sensibility is commonly retained; occasionally there may be complaint of pain in the limbs.

Diphtheritic paralysis affecting the lower extremities, palate and diaphragm.—William C. D——, aged four years. Admitted July 13, 1893. Three months before admission he had diphtheria for fourteen days. During the last two months he seemed to get weaker on his legs; he was noticed to walk as though ‘tipsy. During the last fortnight has been unable to walk more than a few steps. Immediately after the recovery from diphtheria, fluids were noticed to return through his nose. During the last ten days his voice has been weak and so indistinct that his mother could not understand him. Breathing badly for about a week. On admission he does not seem to have very good power of drawing up his legs; the grasp with right hand not so good as with the left; he swallows solid food fairly well, but with a good deal of coughing and spluttering; he cannot cough properly, seeming unable to produce an efficient spasm of the glottis; voice distinctly nasal; he breathes almost entirely with his intercostals. Seems to understand what is said to him, but lies on his back muttering a good deal and not taking much notice of what is going on around. His eyes are generally fixed on vacancy, and the pupils very much dilated. Pupils react to light and accommodation; knee jerks absent. There is no albumen. After admission he gradually recovered, and was discharged well in five weeks.

Very generally these cases tend ultimately towards recovery, but recovery may occupy six months or more. The muscles of the upper extremity in rare cases may become involved, though it is not usual for the loss of power to be as extreme as in the legs. Commonly it is found that the more minute co-ordinate movements of the hands are those which are mainly affected, so that the power of writing is one which is frequently lost. In exceptional cases some weakness affects the muscles of the trunk.

More serious than these, however, are the affections of the respiratory muscles, especially of the intercostals and the diaphragm. Paralysis of the diaphragm is, I believe, very much more common than is generally supposed. In several cases which have been under my care, the condition has been noted, although it gave rise to no obvious symptom of discomfort. In these cases the children have been brought under observation suffering from one or other of the more common forms of paralysis, such as paralysis of the palate and muscles of deglutition, or paralysis of the lower extremities. An early indication of affection of the respiratory muscles may be afforded by some degree of aphonia, and some difficulty in coughing. On examination of a child with paralysis of the diaphragm, the movements of the epigastrium during respiration are seen to be reversed—that is, the epigastrium, instead of rising during inspiration as the diaphragm descends and presses on the abdominal viscera, becomes sucked in more or less, and then returns to its normal position during expiration. In severe cases this failure of action of the diaphragm leads to a marked disproportion between the size of the thorax and that of the abdomen; there is a greater amplitude of movement of the thoracic walls to compensate for the want of movement of the diaphragm, hence the lower costal margin becomes winged and expanded, and below it the abdominal walls seem to fall away. Such an extreme condition is not very frequently seen, but in 1893 it was exhibited in a marked form in a child at the Evelina Hospital, who had been admitted for difficulty of locomotion, due to diphtheritic paralysis, and in whom the affection of the diaphragm developed under observation. The peculiar reversal of the movements of the epigastrium are, of course, due to an ascent of the diaphragm during inspiration, the flaccid diaphragm being drawn up by the elastic force of the lung during its expansion by the work of the intercostal muscles.

Diphtheritic paralysis affecting diaphragm mainly.—Henry S——, aged three and a half years. Admitted February 8, 1894. Diphtheria two months previously. Was in bed for three weeks, then got about for fourteen days, when dyspnœa and great prostration were noticed; generally talkative, but recently has spoken very little; frequent sickness. Fairly well nourished child; apathetic; unable to speak except in a whisper; voiceless cough; palate moved feebly to stimulation; diaphragm did not act; intercostals working and spaces bulging; nasal cry; signs of bronchitis; heart sounds normal but rather feeble; cremasteric reflexes normal; patella reflexes slightly diminished; no paralysis of legs; urine contained albumen. On February 15, diaphragm moved slightly; epigastric angle not so widely opened during respiration; voice improved; much less albumen. On the 19th diaphragm moved well; nasal twang lost almost completely. Recovery slow, but complete.

With regard to the prognosis, when the diaphragm is attacked, a great deal depends upon the time at which the child comes under treatment. Such patients are peculiarly prone to lung troubles, and the paralysis of the diaphragm then presents a serious obstacle to recovery, as the power of efficiently clearing the air passages is interfered with; although the exaggerated movements of the thorax suffice to draw in enough air for the ordinary needs of a healthy lung, they cannot efficiently expand the air cells in the base of the lungs, hence with any engorgement of the lung matters tend rapidly to become worse, while even under the best conditions engorgement is to be expected. Contrary to the statements ordinarily to be met with, my experience is that these patients do not die as the result of asphyxia from paralysis of the muscles of respiration, but from sudden cardiac failure, or from secondary lung complications. (See case of Eliza D. J——, page 107.) Attention being centred upon the diaphragm, the indications of engorgement, of bronchitis, or of pneumonia, may sometimes perhaps have been overlooked, an oversight which is favoured by the frequent development of the complications without any marked rise of temperature. In view of this, it is always advisable to examine the chest frequently, and, so far as possible, to avert these dangers by the avoidance of chills, and by keeping the patient in bed in a warm room.

Paralysis of the intercostal muscles may occasionally be met with when the diaphragm is not involved. I have seen two such cases where the patients were wholly unable to raise the ribs by voluntary contraction of the intercostal muscles. This loss of power lasted three months and led to fears of muscular degeneration, fears which were happily falsified by the recovery of the patients under the influence of strong galvanic currents.

Paralysis of the walls and sphincters of the intestine and the bladder have been described, but such cases have not come under my observation.

With regard to paralysis of the heart, this is more commonly to be regarded as a danger during the primary attack rather than as a form of diphtheritic paralysis occurring during convalescence. Cardiac failure may result from degeneration of the muscular walls, and is to be feared when the pulse, which was previously rapid, becomes small, weak, irregular or infrequent. Sometimes the dangers of cardiac failure may be anticipated from a sudden fall of temperature to considerably below the normal point. In such cases the skin is cold and the face is pale, and the general condition is one of extreme prostration, which may continue a week or ten days before the fatal ending. At other times the cardiac failure may occur suddenly, and be accompanied by fainting attacks. When these supervene the patient may die quite suddenly, or the faint may be succeeded by a period of extreme prostration.

Whether regarded as an accompaniment, a complication, or a sequel, the albuminuria of diphtheria is, I think, mostly regarded in too serious a light. It is true that it is more frequent amongst the fatal than amongst the non-fatal cases; it is true that the degree of albuminuria is, to a large extent, a measure of the severity of the attack of diphtheria; but the occurrence of albuminuria is not an indication of danger of uræmic symptoms, as when this condition supervenes during convalescence from scarlet fever, nor is it an indication that lasting renal changes are to be anticipated. When the question is regarded from the opposite point of view, it is frequently customary to refer certain otherwise unexplained cases of chronic kidney disease to an antecedent attack of diphtheria, but this is, I think, an assumption which is very rarely warranted by the facts of the case. When we judge from the history of known cases of diphtheria, although in exceptional cases albuminuria may be found as late as the tenth or twelfth week, the more usual course is for it to come and go in an irregular fashion until the fourth or fifth week, and then make its final disappearance.

Checking hospital experience by that obtained from insurance work during the past twelve years, although I have seen a very large number of proposers who are stated to have had diphtheria, I have not yet come across a single case in which the diphtheria had left permanent albuminuria; on the other hand, it is, as previously mentioned, relatively rare for no albumen to be found at any time in the course of even a mild case of diphtheria. When it has been found on one occasion it may reappear and disappear without any obvious determining cause. Time after time a varying trace of albumen may be detected, and then a specimen will be examined which fails to give any reaction. Occasionally the albuminuria in mild cases assumes a cyclical character, most of the specimens passed during the day being free from albumen, while those passed near midday or after a meal may contain a fair proportion. In rare cases this cyclical character may persist for several months, or even for a year or two, but the general rule is for albuminuria starting from diphtheria neither to give rise to uræmic symptoms, nor to lead to chronic albuminuria. Although this symptom is undoubtedly of importance when it occurs very early, or when the amount of albumen is very large, it is important as influencing the prognosis of the diphtheritic attack, more than as indicating danger of chronic kidney trouble. Cases thus affected are more likely to prove fatal, but they do not die because of the albuminuria, which appears to serve only as a danger signal; on the other hand, the slight trace which is so often found in most cases of diphtheria seems to be of no importance whatever. The albuminuria is a measure of the degree of internal engorgement, but it is not indicative of any interference with the ordinary eliminative work of the kidney, and it does not point to any destruction of the renal epithelium.

In apparent opposition to what has been said, it might be urged that convulsions sometimes occur in the course of diphtheria, and also that vomiting is not uncommon, especially towards the fatal termination, and these two symptoms might perhaps be taken as indications of uræmia; but against this stands the fact that the convulsions are not of the true uræmic type, and that the vomiting of diphtheria, which is so often associated with an irregular pulse and failure of the heart's action, is not always attended by albuminuria. It may frequently occur with albuminuria, as both symptoms are more common amongst cases tending towards a fatal termination, but the two conditions, vomiting and albuminuria, appear to have no causal relationship. It is, indeed, far more probable that the vomiting, diarrhœa, heart failure, and abdominal pain are the associated expression of a toxæmic neurosis, than that the vomiting is dependent in any sense upon renal changes associated with the albuminuria.

It may be well here to indicate two marked differences between post-diphtheritic albuminuria and post-scarlatinal albuminuria, namely, the colour of the urine and the absence of dropsy. The characteristic red, smoky, scanty urine of scarlatinal nephritis offers a marked contrast to the condition found in the course of diphtheria, where the colour is but little changed, although in very exceptional cases a small quantity of blood may be passed. In fact the appearance and the quantity vary so slightly that, unless the urine is frequently tested, and tested at different times during the day, there may be nothing to point to the presence of albumen. Rarely on microscopical examination casts may be found, but they are more often absent. When present, they are simple hyaline casts, such as may be found with cases of congestive albuminuria associated with heart or lung disease; the casts in themselves afford no indication of structural renal changes. Then with regard to dropsy. This sign is absent as a rule, though the pallor of the face which is so frequent in severe cases of diphtheria may sometimes cause a suspicion of dropsy from the resemblance to the waxy whiteness of the skin in scarlatinal nephritis; but while the pallor is indistinguishable, the true nature of the case may mostly be made out by the absence of œdema of the back or of the lower extremities. It must be remembered, however, that quite independently of albuminuria a slight œdema may sometimes be found when diphtheria has been followed by profound anæmia. This œdema is in its general characters far more comparable to that which is seen so often in badly nourished children, than to the œdema of acute nephritis, which occurs with extreme rapidity and is generally universal.

In a very large proportion of the fatal cases which have come under my observation—whether they have occurred during the primary diphtheritic attack or from one or other of the sequelæ—the notes show that the termination was preceded by sickness and diarrhœa; the former is almost invariable, the latter is very frequent.

Malignant diphtheria with epistaxis.—Joseph M——, aged sixteen months. Admitted October 8, 1890. Difficulty in swallowing; glands in neck much swollen; a deep excavated ulcer on each tonsil covered with white membrane which could not be detached; fauces much injected; discharge from nose. On the 9th profuse discharge from nose when the child coughed. In the afternoon considerable hæmorrhage from mouth and nose after coughing; swallowed with difficulty; some sickness; several loose motions. On the 10th breathing laboured and sucking in of lower ribs; seven loose motions during the night, the last two containing blood; considerable hæmorrhage from nose. Died in the early morning.

The sickness seems to bear no special relation to the nature of food taken, to the mode of its administration, or to the time at which it has been given. It occurs whether the child is fed by the mouth or by the nasal tube, and it always precedes the diarrhœa. Sometimes the patient may suffer from slight sickness for two or three days, and very little anxiety may be felt about the ultimate recovery, but when the vomiting becomes more incessant, a fatal end is to be feared, especially if a previous tendency to constipation is replaced by diarrhœa.

Diphtheritic paralysis; death.—John F. P——, aged two years and four months. Admitted September 18, 1889. When admitted was apparently in a moribund condition, with much sickness and diarrhœa; fluids taken by the mouth returned through the nose. On examination of throat, scars of recent ulcers seen on the tonsils, but there were no signs of inflammation. Some discharge from the ears and enlargement of the glands of the neck. On the 20th neck more swollen, otherwise general condition unchanged. On the 22nd was sick twice. There was a discharge from both eyes, and a film had formed over the left eye. On the 24th squinting was noticed. On the 26th glands in the neck more swollen; diarrhœa excessive. On the 27th the pulse gradually failed, and the patient died.

Sometimes, but not always, the sickness and diarrhœa are accompanied by a distinct complaint of abdominal pain. This pain, which varies considerably in intensity, is mostly referred to the epigastrium. These symptoms almost invariably terminate with cardiac failure, the face becoming paler, and perhaps livid round the mouth, the breathing more irregular and the pulse more rapid and feeble; these symptoms are usually attributed to implication of the pneumogastrics.

While speaking of cardiac failure, it may be well to indicate once more that cases in which the pulse rate varies very widely in a short time are usually to be viewed with uneasiness. Such variations are perhaps of more value during the diphtheritic attack than in the later stages, but whether they occur at the time when the membrane is present, or during the later treatment of any variety of post-diphtheritic trouble, sudden wide variations of the pulse are to be dreaded.

Post-diphtheritic neuritis with pulse changes.—Rose S——, aged five years. Admitted August 14, 1893, with paralysis of palate, internal strabismus and paralysis of diaphragm; semi-apathetic. During the time this child was in hospital the pulse rate was never below 116, and varied between that and 140; pulse extremely feeble at times.

Most of the cases which terminate with gastro-cardiac crises have given warning of an unstable equilibrium, of which an abnormally slow pulse seems to be the chief indication. Sometimes this abnormal slowness is associated with true intermission, sometimes the slowness is replaced for a short time by an unusually rapid pulse; but in whichever of these ways the irregularity of the heart's action is expressed, these cases are to be viewed with anxiety on account of the sudden fatal termination which may occur after any abrupt movement or excitement.

The following case is interesting as illustrating, in a single patient, many of the sequelæ of diphtheria referred to in the preceding pages.

Diphtheritic paralysis; death.—Bertha J. V——, aged five and a half years. Admitted July 4, 1889; died July 10, 1889. Nine weeks ago complained of headache, three days later sore throat. The attack began in the tonsils and spread to the pharynx, but did not interfere with respiration. After five weeks she gained flesh and was able to get about, and seemed convalescent until three weeks before admission, when she became weaker on her legs and fluids were returned through her nose. On admission she was described as a lively child, rather pale and thin, with speech of a peculiarly guttural character, suffering from inability to stand; unable to swallow fluids. *The eye*: all actions of the muscles of the eye are good with the exception of the external rectus of both eyes, which fails to work completely. When an object is placed to the outer side of either eye, the internal rectus draws the further eye inwards, while the eye nearest the object looks straight forward. Reaction to light and accommodation is good. *Reflexes*: There is no patella or ankle clonus. The patient feels when touched at any part, and can designate the spot. The muscles of expression work normally. All movements of the limbs can be performed, but rather sluggishly, but the patient is unable to stand on her legs. When attempting to swallow fluids, she takes very little at a time, and some returns through her nose. Speech is guttural, husky and indistinct, but one is able to understand what she says. When lying down in bed she is unable to get up or sit up of her own accord, but has to be raised. When once sat up, she can maintain her position without support. Temperature on admission 97·8, pulse 120, respiration 32. On July 6 she is reported as sleeping fairly well, but crying out and starting occasionally. Loose cough, slight discharge from both eyes, some complaint of pain in knees; no return of fluid through the nose; the bowels have not acted since admission. July 8: Yesterday afternoon there was great difficulty in inducing the child to take some brandy and egg mixture, which was returned immediately by the nose. In the evening the pupils were widely dilated. A nutrient enema was given at 1 A.M., but was returned after half an hour; the nasal tube was now used for feeding. The diaphragm does not appear to be acting constantly, although at times it acts quite well. The breathing occasionally becomes distressed and the child gets blue. July 9: She seems a great deal better. Nose bled slightly last evening; breathing laboured, loud and irregular during sleep. This morning breathing regular, and the child is better and brighter. The deltoid muscles in both arms seem paralysed, and the child is unable to raise the arms at right angles to the trunk. July 10: In the night she had attacks of dyspnœa after feeding, and after one severe attack at 10.30 A.M. she succumbed, in spite of artificial respiration. No post-mortem was permitted.

CHAPTER IV

DIAGNOSIS AND PROGNOSIS OF DIPHTHERIA

The diagnosis of diphtheria.—Few things in medicine are so difficult as the accurate recognition of diphtheria in the earlier stages; few diseases give rise to such frequent mistakes, and a mistake, when it occurs, is likely to cause considerable pain to the friends, whether the diagnosis of diphtheria is too hastily made and therefore anxieties unnecessarily aroused, or if the nature of the disease is overlooked during the first stage, and a cheerful, hopeful diagnosis is made which is doomed to later correction. The diseases with which it may be confused may be so simple and so trivial, while diphtheria itself is frequently so dangerous, that it is essential to form a diagnosis as early as possible.

Until the discovery of the importance of the Klebs-Loeffler bacillus, the diagnosis frequently presented considerable difficulty, and even since the connection of this bacillus has been recognised, numerous cases have been found to present all the clinical features of diphtheria although the bacillus may be absent. Speaking broadly, the recognition of the disease is mostly to be based upon the recognition of the pseudo-membrane. If time allows for bacteriological investigation, the nature of many cases of doubt may be cleared up by the recognition of the bacillus; but some cases in which the bacillus is found to be present would otherwise give rise to no anxiety, while, on the other hand, in some cases of undoubted diphtheria clinically, the bacillus is sought in vain. It is doubtless wise in every case of doubt to endeavour to obtain cultivations of the bacillus and to submit these to microscopical examinations, but a large number of cases when they are first seen are so urgent that treatment must be commenced regardless of bacteriological research, and in such cases a provisional diagnosis must be made on the general clinical aspect of the case. Frequently considerable assistance may be afforded in doubtful cases by a consideration of the age of the patient (diphtheria, as has been previously indicated, being much more common in the earlier ages of life); the recent occurrence of throat affections amongst other members of the family; evidence of similar affections in the house or the neighbourhood will also furnish very material assistance; and in the case of school children inquiry should be made about the frequency of illness in the school, and the possibility of infection from the surroundings. The sanitary condition of the house in which the patient lives should also be inquired into, although this is of minor importance except as a predisposing cause. Still, when all such points have been investigated, it must be remembered that numbers of mild cases remain doubtful throughout their course, and the true nature of the disease may sometimes only be established by the occurrence of one or other of the sequelæ of diphtheria.

The appearance of the throat will often afford some help during the early stages, although the existence of patches of membrane upon the tonsil may frequently, during the first day or two, leave the question of diagnosis open. When the patches detach, the nature of the disease may sometimes be inferred from the appearance of the tonsil, but before the detachment of membrane, the spread of the exudation over the pillars of the fauces, or over the palate and uvula, will indicate the nature of the disease. Still, it must be remembered that in many cases of mild diphtheria the membrane from the beginning to the end of the disease is located purely on the tonsil; when it invades the posterior wall of the pharynx, or the post-nasal space, there can be no doubt in the majority of cases that we are dealing with diphtheria, and this is rendered more certain by any indication of coryza or rhinitis, which are never seen with cases of simple sore throat. The rhinitis is in such cases marked by a thin, purulent secretion, which is especially noticeable during crying or other expiratory efforts, and the secretion appears to be peculiarly irritating, so that the nostrils and the upper lip are frequently reddened and sore. The frequency of rhinitis in cases of malignant diphtheria has already been alluded to, and it must be regarded as an indication of considerable danger, although since the introduction of antitoxin the mortality in such cases has been considerably reduced. The cases of the greatest difficulty are those in which the membrane is not visible at the earliest examination of the child, and in these a provisional diagnosis can only be made by consideration of the temperature, the pulse and the general condition. The range of temperature is usually low as compared with other affections of the tonsils, and the temperature as a rule falls to normal or even to subnormal when the membrane has been fully formed. Variations in the temperature will only be associated with implication of the glands or with the development of any of the common complications of diphtheria, but even during pneumonia the temperature does not always follow the characteristic course of pneumonia independent of diphtheria ; since the prominent feature of the disease is asthenia, the temperature rarely follows a typical course. The rapidity of the pulse and its disproportion to the temperature are also common indications of the true nature of the disease, while the general condition of the patient is marked by depression and asthenia, which are frequently greater than the local appearances would account for, if the case were one of simple tonsillitis.

Cases of laryngeal diphtheria present greater difficulties, since in these it is frequently impossible to obtain a view of the larynx. The diagnosis may be favoured by the existence of an epidemic of diphtheria, by the gradual onset of the symptoms, and by the progressive evidence of stenosis. If at the same time the temperature is low instead of high, and the pulse is abnormally rapid, a provisional diagnosis may be made before portions of membrane have been expectorated. The diagnosis in such cases lies between diphtheria and catarrhal or spasmodic laryngitis, and it is obviously necessary when in doubt to treat the disease as one of diphtheria. Sometimes cases of abscesses in the neighbourhood of the larynx, or tumours of the larynx, may present difficulties, while a suspicion of the presence of a foreign body in the air passages may occasionally be aroused, until the history of the case has been investigated.

As the diagnosis of diphtheritic sore throat depends so largely upon the presence and the appearance of the membrane, it becomes important to consider other diseases in which membranes not unlike those of diphtheria may form upon the tonsils or the fauces. Not only are such membranes formed in the course of numerous diseases, but they may result from various forms of irritants which have been locally applied, the membranes which result from the intentional or accidental administration of strong preparations of various poisons, such as nitric acid, carbolic acid, nitrate of silver, are extremely like those of diphtheria on cursory inspection, and similar membranes may result from the accidental inhalation of steam, or, in rare cases, from attempts to swallow boiling water. In these, although the appearances are somewhat like those of diphtheria, the membrane is usually more widely diffused, and there is almost always a definite history of the cause. Thus the membrane forms rapidly in children who have been inhaling steam from the spout of a kettle, and the local symptoms predominate, while the history points to the sudden onset following immediately after the accident. So, too, with the various irritant poisons. Not only will membranes be seen on the tonsils and fauces, but there are usually also large white streaks to be seen on the tongue and on the cheeks indicating the passage of the irritant over the mucous membrane. It is only when the membrane results from the local application of caustic that the appearances may be misleading, but in these the history is always conclusive.

Of conditions with which the formation of false membranes are associated the following may be mentioned:—Follicular tonsillitis, scarlet fever, measles, typhoid fever, small-pox, chicken-pox, and herpes of the tonsil.

Follicular tonsillitis is perhaps the disease which is most frequently confused with diphtheria, and there appears to be little doubt that many cases of so-called follicular tonsillitis are really diphtheritic, the nature of the disease being made manifest at a later stage by the occurrence of various sequelæ. On the other hand, the membrane in follicular tonsillitis does not spread over the fauces; it is usually limited to the tonsils, and commences commonly as numerous scattered white patches which tend gradually to fuse. In follicular tonsillitis the temperature is usually higher than in diphtheria, and it remains high for a greater length of time, and is rarely followed by the fall below normal which is so frequently seen in diphtheria.

When an epidemic of scarlet fever co-exists with one of diphtheria, the nature of the disease is very frequently obscure in the early stages. The sore throat of scarlet fever is often characterised by the appearance of a false membrane, and the lymphatic glands are enlarged at an early stage. It may be pointed out that in scarlet fever the submaxillary glands are somewhat more prone to be affected than the cervical glands; also that the inflammation is usually more intense in scarlet fever, and that the glands are more likely to suppurate at an early stage. The larynx very frequently remains free from infection, although cases have been mentioned in which an extension of false membrane was found in the larynx. The exudation in scarlet fever is usually more discoloured in the early stages, being yellowish or more grey than in the early stages of diphtheria, where the membrane is usually of a semi-transparent, white character. The membrane in scarlet fever tends also to liquefy into a purulent mass, and on separation is prone to leave deep destructive ulcers. The onset of scarlet fever is usually marked by more severe symptoms than the onset of diphtheria. Vomiting may occur early, while the vomiting of diphtheria is usually a late symptom, one, indeed, which commonly precedes a fatal termination. The temperature of scarlet fever is usually higher than that of diphtheria, and the appearance of a rash will of course in the majority of cases be quite conclusive, although a rash somewhat like that of scarlet fever occasionally occurs in the course of diphtheria. The diphtheritic rash very rarely appears as early as the rash of scarlet fever. In scarlet fever sanious discharge from the nose is not common, but during the ulcerative process hæmorrhages from the throat may occur. Scarlet fever may, however, be complicated by diphtheria after the second or third week, the damage to the tonsil appearing to have favoured the reception and development of the bacilli of diphtheria. Such cases are usually severe, but the severity results from the asthenia of diphtheria being superadded to the weakness produced by scarlet fever. Unless true diphtheria has occurred in this way, as a complication of scarlet fever, paralysis is not to be feared. In scarlet fever when the inflammation extends to the air passages it is comparatively rare for a membrane to be formed. Laryngeal symptoms may ensue as the result of acute œdema, consecutive to the ulceration of the tonsils, but the symptoms are practically indistinguishable from those of laryngeal diphtheria.

In the course of measles indications of soreness of the throat may sometimes be found, but the early symptom of coryza and the redness of the conjunctivæ usually serve to render the diagnosis clear. The early stages of measles are also characterised by the tendency to pulmonary symptoms. In exceptional cases a membrane may appear upon the fauces, but this is not likely to be followed by any ulceration of the throat. As in the case of scarlet fever, true diphtheria may occur as a sequel of measles. Measles being characterised by a tendency to affection of the air passages, we find that laryngeal symptoms are much more common than in scarlet fever, while acute membranous laryngitis is even more common than in true diphtheria.

It is improbable that the early stages of typhoid fever can ever be mistaken for the onset of diphtheria. The course of the temperature, the headache and the characteristic diarrhœa render most cases of typhoid fever sufficiently easy to recognise, but towards the third week some irritation of the fauces occasionally occurs, and may be followed by the formation of a membrane which is characterised by not increasing in thickness and by not separating easily. Although this false membrane may occasionally occur independently of diphtheria in the course of typhoid fever, true diphtheritic attacks are sometimes to be met with. Murchison has indicated the seriousness of laryngeal symptoms in the course of typhoid fever, and he has shown that the laryngitis occasionally leads to ulceration of the mucous membrane of the larynx or trachea. He agrees with Trousseau in saying that these cases are most apt to occur when there is unusual predisposition, when the disease has been very protracted, and where the diet has been very rigorous. He says that several examples of enteric fever complicated with diphtheria have come under his notice, and he mentions eleven cases that have occurred in the practice of other physicians. He gives the details of a case in which there was also albuminuria and paralysis of the pharynx. The case was that of a young man aged 22, who had been ill with fever and diarrhœa for a fortnight before admission. After admission the diarrhœa continued and typhoid spots appeared. On the thirty-fifth day of the disease it was found that the patient had difficulty in swallowing, apparently owing to paralysis of the pharynx. When an attempt was made to swallow fluids, a great part was rejected by the nostrils, the dysphagia increased, the breathing became rapid and embarrassed, and the countenance dusky, and notwithstanding treatment the patient died on the thirty-sixth day. At the autopsy numerous small ulcers were found at the lower end of the ileum, most of them cicatrising; the spleen weighed ten ounces, and was soft; both kidneys were large, smooth and congested; cortices hypertrophied and opaque, the weight of both together seventeen ounces; the urine in the bladder contained a good deal of albumen; the epiglottis and upper third of the larynx swollen and red, and the mucous membrane covered with a continuous, thin, false membrane, becoming broken up into shreds at its lower margin; no ulceration; both lungs were congested, with a few scattered patches of lobular pneumonia.

A similar case of true diphtherial croup occurring on the fourteenth day after admission for typhoid fever has been recorded by Dr. Gayton in the 'Lancet,' May 5, 1894. The symptoms necessitated tracheotomy, and the child made a good recovery. In rare cases of typhoid fever false membranes may occur upon the fauces at an early stage of the disease, and in these it usually disappears after a few days. The appearances may be misleading, but the temperature chart is usually to be trusted to clear up the diagnosis.

In ordinary cases of small-pox, membranous exudations appear never to occur, but they have been seen in rare cases of a malignant type, and are then associated with deep ulcerations and sometimes with œdema of the glottis.

Thin, membranous exudations occasionally form in the course of chicken-pox and present no difficulties on account of the obvious nature of the attendant symptoms.

Herpes of the palate or of the tonsils sometimes causes the appearance of false membranes, but these are characterised by being limited to the spot first affected, and by the absence of any tendency to spread. With herpes, the diagnosis may sometimes be aided by the concurrent appearance of herpes on the lips, the cheeks, or the tongue.

In all of the above diseases some material assistance may be derived from bacteriological examinations; but the attendant symptoms, the appearance of a rash, the definite course of temperature, and other characteristics of the specific fevers rarely leave any doubt after the case has been seen two or three times.

Prognosis of diphtheria.—Although the diagnosis of diphtheria presents many difficulties which can only be removed by most careful consideration of all the features of the case, when once the nature of the disease has been recognised, anxiety is aroused which is continued throughout the acute stage and for a lengthened period subsequent to apparent recovery. Diphtheria differs from nearly every other disease in this prolongation of anxiety and uncertainty; even when the symptoms show signs of improvement it is always well to speak with caution about the ultimate recovery of the patient. This caution should extend not merely to the question of life or death, but to the dangers incidental to the various sequelæ. The prognosis of diphtheria is necessarily dependent upon the nature of the attack, upon its extent, the site affected, and upon the various complications and sequelæ. These have already been dealt with in detail under the headings of 'Symptoms' and of 'Complications and Sequelæ,' but their special prognostic significance may perhaps with advantage be here summarised.

It is by no means uncommon for sudden death to occur even when most of the symptoms appear to point towards recovery, therefore it is necessary to weigh carefully every symptom and all the conditions connected with the case before forming a prognosis of too hopeful a character. In attempting to form an estimate of the danger, regard must be paid in the first place to the age of the patient. Not only is diphtheria a disease which is most common during the earlier years of life, but it is also most fatal during that period. From the tables recently published by the Metropolitan Asylums Board, it would appear that out of 3,042 cases which occurred during the year 1894—that is, previous to the employment of antitoxin—the general mortality amounted to 29·6 per cent., but of these 3,042 cases 1,171 occurred before five years of age, and in these the mortality amounted to 47·4 per cent., the exact mortality for the different ages being 62·1 per cent. under one year, 61·7 per cent. from one to two, 51·3 per cent. from two to three, 47 per cent. from three to four, and

31·1 per cent. from four to five. Of the 1,075 cases which occurred between the ages of five and ten years, the mortality was only 26 per cent.; while of the 363 cases which occurred between the ages of ten and fifteen years, the mortality fell to 11·2 per cent.; of the 160 between the ages of fifteen and twenty, the mortality fell to 4·3 per cent.; while of the 273 cases aged twenty and upwards, the mortality was only 6·5 per cent. The greatest mortality therefore occurred during the first two years of life, although the range was still very high between the ages of two and four. These general results agree closely with those given by Mr. Lennox Browne, who found the mortality in 1,000 cases 45 per cent. under five years of age, 26·2 per cent. from five to ten, 11·7 per cent. from ten to fifteen, and 3·88 per cent. over fifteen. Very little can be said of the relative death-rate in male and female children, for the increase in the numbers affected is mostly associated with an increase in the mortality.

Then with regard to the local conditions of the individuals affected, there is no doubt whatever that the disease is peculiarly fatal amongst the upper classes, death occurring in these cases very early in the course of the disease. If, however, regard is paid to the prospects of recovery during the later stages, the children of the well-to-do appear to stand a far better chance; they convalesce more rapidly, and they suffer from the sequelæ less commonly; and even when sequelæ have been developed, the tendency to recovery is greater than amongst the poorer classes, where the unsanitary surroundings and the deficiency of proper nourishment will largely influence the restoration to health.

Different epidemics differ very widely in severity, and the prognosis must always be influenced by the prevailing character of the epidemic. During the early days of the treatment with antitoxin it was frequently asserted that the apparent improvement of the results of treatment were due to the prevalence of a mild type of diphtheria. This suggestion, however, has not been borne out by more extended observations, and although cases of this disease are always serious, the estimate of danger in any particular case must be influenced by the knowledge of the existing mortality from diphtheria in the surrounding district.

In the individual case the prognosis will to a great extent depend upon the various symptoms presented by the patient. Thus the danger of the case will in the early stages be dependent upon the anatomical distribution of the membrane. The greater the amount of surface affected by the membrane, the greater will be the danger. From a large surface toxalbumins will be likely to be absorbed to a great extent, and when a large surface is affected there may be danger of interference with respiration. It may be broadly stated that the danger is greatest when the nasal passages or the larynx are affected in addition to the fauces. When confined to the fauces the mortality is relatively low, while it is high if confined to the nasal passages. It will be remembered that the so-called malignant form of diphtheria is that in which the nasal passages are mainly affected, and indeed Trousseau speaks almost despairingly of cases of nasal diphtheria associated with much glandular engorgement. He predicts that in most cases a state of prostration is reached in which the child refuses every form of food and drink. With laryngeal cases there is necessarily a twofold danger to be feared, the danger of death from asphyxia in the early stages of the disease, and the danger of death from the development of pulmonary symptoms at a later stage.

The prognosis will also be influenced to a certain extent by the appearance of the membrane. When it is of a dark, gangrenous appearance, and when the masses of exudation break down readily, there is considerable danger of the absorption of poison from the affected surface. These cases are frequently characterised by a foul odour from the mouth, and by a yellowish or blood-tinged acrid secretion from the mouth and from the nose: and in addition the serious nature of the case may frequently be inferred from the large amount of swelling, tenderness and redness of the lymphatic glands in the neck and of the surrounding cellular tissue. Even when the disease has been confined to a small portion of the fauces the dangers of extension to the larynx and to the nose must be remembered. It is by no means uncommon for cases that have apparently been progressing towards recovery to undergo relapses, which are always serious owing to the weakened condition of the patient.

Independently of danger from obstruction to respiration, a sudden fatal termination of the case may occasionally occur from paralysis of the heart, which may supervene at almost any stage of the disease, and which frequently occurs almost without warning, even during the time of apparent convalescence.

The symptoms of danger which may be developed in the early stages of the disease are those indicative of the profound asthenia of the patient. These usually occur after the second or third day, and are characterised by the pallor and sometimes by the almost œdematous appearance of the face, and by the general listlessness and apathy of the patient, who refuses to take notice of friends or of playthings, and lies in a state of torpor. Other symptoms of danger are the occurrence of vomiting and diarrhœa, but these usually occur somewhat later, while depression of temperature below normal is also indicative of asthenia, and may sometimes be of serious prognostic value. The development of purpura and any tendency to hæmorrhages will also cause anxiety. In every case of diphtheria the pulse must be watched closely. It has been previously pointed out that the characteristic of the pulse in diphtheria is the extreme rapidity as compared with the temperature, the rapidity being due to the asthenia rather than to any rise of temperature. A rapid pulse which does not present any wide variations from day to day is not in itself an unfavourable symptom; but if the pulse presents great variations in rapidity, and if it becomes irregular in force and in rhythm, cardiac failure is to be feared. Sir William Jenner long since pointed out the dangers of an extremely rapid and feeble pulse, and the purity of the heart's sounds will frequently be found to be impaired when the pulse increases in rapidity and in weakness; but on the other hand a markedly slow pulse, when it occurs without any sign of improvement of the other symptoms, is frequently of fatal significance. Extreme restlessness is always to be viewed with anxiety, and it frequently forms the prelude to death, in a condition of delirium or of general asthenia. When the patients refuse their food the prognosis becomes grave; to a certain extent this anorexia may be counteracted by treatment, but the danger of slow exhaustion and of progressive and extreme emaciation is one which is frequently associated with malignant cases, and in these, in spite of treatment, the anorexia may give place to vomiting and diarrhœa unless extreme care is taken with the feeding by the nasal tube.

Of the various sequelæ, the different forms of diphtheritic paralysis vary largely in importance, the prognosis depending partly on the degree of paralysis, and partly on the muscles affected. Thus, when pharyngeal muscles or extremities are involved the prognosis is usually favourable. Mild forms of diphtheritic paralysis usually tend towards recovery; but, on the other hand, if the muscles of respiration are affected, the dangers of pulmonary complications depend largely upon the surrounding conditions. If it is recognised that the diaphragm or the intercostals are affected, and if the patient can be kept recumbent in sanitary surroundings, the risks to life may be considerably reduced; but in these cases there is always danger lest the diphtheritic process should involve the cardiac nerves or the tissue of the heart, when alterations in the pulse must be anticipated, and there is danger from sudden cardiac failure.

Of the other forms of diphtheritic paralysis, those affecting the ocular muscles, or the bladder, or rectum give rise to little fear of danger, and with regard to the albuminuria which occurs, this, as has been previously pointed out, is not in itself a danger, although it is frequently indicative of a malignant type of the disease. Cases of death from coma and convulsions have been attributed to uræmic poison; but, unless the urine is suppressed, there appears to be little danger of serious symptoms resulting from the albuminuria, either during the diphtheritic attack or from the development of permanent renal affection.

CHAPTER V

GENERAL AND MEDICINAL TREATMENT OF DIPHTHERIA

Treatment of diphtheria.—The whole of the treatment of diphtheria has, within the last few years, been very materially influenced, first by the discovery of the importance of the Klebs-Loeffler bacillus, and secondly by the observations of Behring, Aronson, and others, of the value of diphtheritic antitoxin. Previous to this few diseases had been treated with such varying results; in fact, before the introduction of antitoxin, medical literature teemed with records of the virtues of various new specifics for diphtheria. Perhaps few diseases have been treated by such numerous remedies, and for every remedy a large percentage of success has been claimed. With diphtheria, as with whooping cough, it has been found that the drugs recommended were first vaunted greatly, then they gradually fell into disuse until, perhaps, they were completely forgotten; and a few years later they were introduced again as novelties with the same extravagant praise and a similar list of successful cases. Henoch stated in 1874 that, according to his experience, all the remedies hitherto recommended were of no use whatever in severe cases of the disease, and he further said that it was only in such that they were wanted, for the slighter cases recovered without treatment; and even in the fourth edition of his book on children's diseases, published fifteen years later, he repeated the opinion originally expressed—in fact, he considered that in really severe cases almost every form of treatment was absolutely worthless.

Even before the discovery of the bacillus, the opinion was gaining ground that the disease depended upon the growth of bacteria, and the treatment was largely influenced by various attempts to destroy the activity of the bacteria by various antiseptic remedies. Most of the remedies have been recommended for local application, and much difference of opinion has been expressed as to the best way of applying antiseptics locally. Some writers maintain that the membrane should always be first removed before the employment of any local application, while others appear to regard the membrane almost with superstitious reverence, as a thing that is not to be interfered with in any way. Still, in spite of the great differences of opinion concerning the appropriate antiseptic to be employed, there was general agreement upon certain lines of treatment. Broadly it may be stated that, independently of the antitoxic treatment, the treatment of the disease may be considered under the following headings: (1) The hygienic treatment; (2) constitutional treatment; (3) local treatment; and (4) symptomatic treatment.

Hygienic treatment.—Concerning the hygienic treatment, the patient is necessarily to be isolated from other inmates of the house, and it is well in selecting a room for the patient to consider the possibilities of securing abundant light, free ventilation, and even temperature. Light is essential not only on account of the possible need of surgical interference at a later stage of the disease, but it is also necessitated by the general depressing influence of the disease. Any disease of a depressing nature requires the cheering stimulus of bright surroundings, while the influence of direct sunlight assists ventilation very materially. Although cheerful surroundings are required, all unnecessary curtains and hangings should be removed, as these might tend later to spread the disease, and they also interfere considerably with ventilation. The temperature of the room is necessarily dependent somewhat on the season, but care should be taken to preserve an even temperature so far as possible. Ordinary cases appear to do best with a temperature of from 65° to 70° F. There is a general tendency to keep the rooms of diphtheritic patients too warm, and it cannot be too often insisted upon that by unduly raising the temperature of the room we may seriously interfere with the freedom of respiration. In severe cases the need of fresh air is extreme, and care should always be taken to supply an adequate amount of fresh air independently of cold draughts. Sometimes, especially in laryngeal cases, there appears to be some advantage in employing a steam kettle so as to render the air in the room more moist, but it is never necessary to surround the patient with a steam tent and to saturate the air inside the tent with moisture; after tracheotomy it may be necessary sometimes to use the tent and steam kettle, but the nozzle of the tube should be placed near the foot of the bed, while the tent should be freely open on one side. This is essential not merely for the purposes of ventilation, but also for the convenience of nursing. Diphtheritic patients require constant watchful care, which can scarcely be furnished if the curtain of the tent has to be raised repeatedly. From the beginning it is necessary to maintain perfect quiet. The patient should be kept on his back and not allowed to raise his head. In many cases, however, this injunction is almost superfluous, the patient is so weak that he shows no tendency to get up. In the most severe cases the tendency to restlessness must be prevented, so far as possible, by loops of webbing passed round the armpits and across the body. It is scarcely necessary to say that no patient with diphtheria should be left without a nurse either night or day, and, notwithstanding the natural feelings of the friends, it is generally advisable that a trained nurse should be employed, owing to the extreme risk of the spread of the disease amongst those who are influenced by affection for the patient rather than by interest in the case. In my own experience it is extremely rare for the disease to spread from patient to nurse, while, on the other hand, the spread from patient to relative is lamentably frequent. Further than this, it is well to impress on the friends and relatives that patients with diphtheria are usually more amenable to the quiet influence of a nurse, who is able to restrain some of the restlessness by the power of her authority. The customary measures of isolation and the free use of antiseptics should be carried out just as in dealing with a case of scarlet fever.

Constitutional treatment.—With regard to constitutional treatment, it may be broadly stated that in all cases of diphtheria the treatment should be directed to counteracting the depressing influence of the disease, hence nourishing food in a liquid form should be administered freely, and in nearly every case it is necessary to employ alcohol with a liberal hand. Food and medicine must be administered with a feeding cup so as to avert any risk of disturbance of the circulation from sudden changes of position. The amount of alcohol taken will necessarily depend upon the degree of prostration. Some practitioners prefer to employ champagne, especially if there is any tendency to vomiting. In my own cases I employ brandy in repeated small doses, so as to maintain a moderate stimulant action. Even when employing alcohol in this way it may sometimes be necessary to give larger doses occasionally, the indications for this being found in the state of the pulse or the appearance of the face. No definite rule as to the quantity of stimulant to be employed can be laid down. The brandy should be commenced early in almost every case, and the amount should be regulated by the nature of the pulse. In severe cases, when the pulse shows signs of failure, other forms of cardiac stimulants should be employed, such as digitalis, strophanthus and strychnine according to the urgency of the case. These may be administered either by the mouth, or, in the case of strychnine, by hypodermic injection. When employing digitalis for diphtheria, it is necessary to remember its cumulative power and to reduce the dose as early as possible. In mild cases there appears to be some advantage in the use of perchloride of iron, which may be given in combination with phosphoric acid and glycerine. It is rarely well to employ large doses of this, on account of the tendency to interfere with digestion; small doses of from one and a half to five minims of the tincture, according to the age of the child, may be given, well diluted. Another remedy which is frequently employed is chlorate of potassium, but this should only be used when the child is old enough to use it as a mouth-wash. In infants there is some danger of producing toxic renal symptoms if the drug is used in a large amount. Carbolic acid is preferable to chlorate of potassium, and this may be employed either as a local application or in the form of a spray. Dr. Gee recommends the use of a solution of carbolic acid of the strength of 20 per cent. for children and of 30 per cent. for adults, employing glycerine, castor oil, and rectified spirit as solvents. He speaks in terms of praise of the value of sulphoricinic acid as a vehicle, and he advocates the detachment of the membrane by some close, soft material before applying the solution to the denuded surface. In pharyngeal cases much comfort is often derived from sucking small lumps of ice; the application of cold in this way serves to numb the fauces, and to allow food to be taken with greater ease.

Local treatment.—With regard to the local measures that have been adopted, these are almost too numerous to mention. In Hare's 'System of Practical Therapeutics' no less than forty-two drugs and methods of treatment are mentioned as having been recommended during the preceding twenty years. The main ideas connected with the local treatment of diphtheria consist of the destruction of the germs upon which the disease depends, either by the use of escharotics or by antiseptics, while some substances have been vaunted as solvents of the membrane. The treatment by escharotics has now to a large extent been discarded, but it may be mentioned that various strong acids and nitrate of silver have been used locally to destroy the membrane. There can be no doubt that the antiseptic treatment has been gaining in favour of late years, and to be effective the antiseptic must be repeatedly applied at regular intervals. After the membrane has been detached and the antiseptic has been applied, the membrane tends speedily to re-form. Some writers are strongly averse to any interference with the membrane, and their arguments in favour of letting the membrane alone are based upon two considerations—first, the risk of damaging uninfected portions of the mucous membrane, and so presenting an increased surface for the development of fresh membrane; and, secondly, detachment of the membrane is believed to be useless by those who hold that the germs upon which the disease depends have already passed into the lymphatics and blood vessels, and are therefore beyond the reach of local treatment. This assumption would, however, tell against the employment of any local measures. Of the supporters of modern views of the true nature of the disease, Professor Watson Cheyne considers diphtheria is from first to last a local disease, the general symptoms being merely due to chemical poisoning ; and to those who hold this view of the disease local treatment must necessarily appear beneficial, and if local treatment is to be adopted at all, there can be no doubt that it is most effective when the false membrane can be detached as much as possible and the application made to the denuded surface. The detachment of membrane may sometimes be effected by careful use of the forceps, but more generally it is safer to rub off the membrane with a gentle use of swabs of soft lint and absorbent wool mounted on vulcanite rods. Some practitioners prefer to cover the index finger with lint and employ gentle friction over the diseased surface.

The local application most employed is lactic acid, either of the pharmacopœial strength or diluted with three parts of distilled water. This may be applied either by means of a brush or as a spray to the affected parts, and it appears to favour the detachment of the membrane, and also to be inimical to the further formation of membrane. Dr. Goodhart prefers a saturated solution of borax with soda or boracic acid in glycerine, and he speaks favourably also of the value of permanganate of potash of the strength of twenty grains to the ounce, and of a solution of quinine ten grains to the ounce made by the aid of hydrochloric acid and dissolved in equal parts of glycerine and water. Other writers are in favour of the use of perchloride of mercury, dissolving one part of corrosive sublimate and five parts of tartaric acid in 1,000 parts of water. When this solution is used, the diphtheritic patch is first cleansed with a wad of cotton, and the bleeding surface is swabbed thoroughly with the solution. Amongst the benefits claimed for this form of treatment is the fall of the temperature after the second or third application. The biniodide of mercury solution has been highly praised by Dr. Illingworth, whose formula is—

R. Liq. hydrarg. perchlor.	ʒiij
Potas. iodid.	gr. x
Ferri et ammon. cit.	gr. xx
Syrupi	ʒiv
Aquæ	℥ij

In 1891 satisfactory results were reported from the paraffin treatment of diphtheria. The ordinary paraffin used in lamps is applied by means of a large camel's hair brush to the raw surface every hour. I must confess, however, that in my practice this treatment has not given very satisfactory results. I have derived more satisfaction from the use of sulphur insufflations, a small quantity of sulphur being blown through a small tube upon the denuded surface.

Other remedies that have been recommended for local employment are a mixture of sulphurous acid and glycerine, liquor sodæ chlorinatæ of the pharmacopœia, and chlorine water. Dr. Gee recommends the use of a spray of saturated solution of boric acid, while peroxide of hydrogen has been much recommended as a topical remedy in diphtheria, the main objection to it being its unstable character. Simple astringents have been used, but can exert no specific action, and in a serious disease like diphtheria they appear to be inapplicable. Many forms of solvents have been recommended; some consist of alkaline solutions, such as the bicarbonate of potash or soda, while pepsine, papaïn, and resorcin are said to possess special solvent properties. Experiments made at the Evelina with solutions of these did not confirm the statements of their solvent properties. Portions of membrane have been kept in solutions of papaïn for many hours without undergoing any apparent change. Sometimes it is difficult to use sprays or irrigations in cases of pharyngeal diphtheria, and in such cases Dr. Dillon Brown, of New York, advocates the inhalation of fumes obtained by subliming calomel.

When solutions are employed in the local treatment of pharyngeal cases it is generally advisable that they should be of a fairly high temperature. Whatever form of solution is used should be employed rather liberally, as water in itself is a cleansing agent and appears to dissolve the toxins of diphtheria. It has been pointed out that the solvents so often employed in antiseptic throat washes—alcohol and glycerine—in all probability interfere with the germicidal properties of mercury and carbolic acid. For the relief of pain due to swollen glands warm applications to the throat, either poultices or warm fomentations, have been frequently recommended, but, unless pus is forming in the cervical or submaxillary glands, warm applications are better avoided, on account of the discomforts produced by the weight and the absence of any compensating relief. When the adenitis has proceeded to the formation of pus, and especially when an operation has been necessary to evacuate the pus, warm applications become essential. In most cases much relief of pain and diminution of inflammation can be effected by the continuous use of ice-bags or Leiter's coils; the latter especially give good results and are cleanly and easy to use.

In nasal diphtheria and post-nasal diphtheria many of the remedies which have already been mentioned may still be applied, and in these cases considerable importance attaches to local cleanliness. The nasal passages may be treated with gentle douching, spraying or syringing with diluted solutions of chlorate of potash and glycerine, or of borax and glycerine. These appear not only to cleanse the surface, but also to be soothing. Dr. Dillon Brown lays stress upon the importance of keeping the nozzle of the atomiser exactly in the middle line of the nares, so as to avoid risk of injury to the septum or inferior turbinated bone, and consequent epistaxis. It is well to remember, in treating cases of nasal diphtheria, that the tendency to asthenia is very great, some of the gravest cases of diphtheria being those with ichorous discharge. Not only is the disease graver in itself, but local treatment is more difficult to apply. In these cases the free employment of drugs and measures intended to relieve the asthenia becomes a matter of urgent necessity. Cases of nasal diphtheria are said to be more common amongst children with adenoid growths, and in such cases the disease spreads rapidly and the interference with the breathing is likely to be extreme. The general internal treatment must be conducted as in pharyngeal diphtheria, but the need of stimulants is generally greater.

When aural diphtheria occurs as a complication of pharyngeal diphtheria, special treatment may be necessary. The early indications of this extension are the occurrence of pain in the ear, which should always lead to an examination of the tympanic membrane. Early operative interference may frequently prevent destructive changes leading to chronic otorrhœa. In addition to early operation much benefit may be derived from frequent use of Politzer inflation; this in combination with syringing with warm solutions will tend to cleanse the Eustachian tube and possibly to avert later dangers. Sometimes, in spite of local treatment, symptoms of inflammation develop, such as tenderness over the mastoid region, with redness and swelling. Under such circumstances it is necessary to make an incision over the mastoid process down to the periosteum. It is rarely necessary to open the mastoid cells.

Ocular diphtheria—that is, the formation of membrane on the conjunctiva—has been described by Mr. Lennox Browne as a very rare event, but I have seen several such cases at the Evelina and at King's College Hospital. Cohn of Breslau recommends the frequent application of a 5 per cent. solution of benzoate of sodium. My own practice has been to employ warm douches to keep the surface of the conjunctiva as clean as possible, and to inject antitoxin.

CHAPTER VI

TREATMENT OF LARYNGEAL DIPHTHERIA: INTUBATION AND TRACHEOTOMY.

Laryngeal diphtheria.—The treatment of laryngeal diphtheria really forms the most important subject connected with this disease, as in these cases the changes are rapid, and children who appear at one moment to be doing well may suddenly present symptoms of extreme urgency. It is essential, therefore, to watch closely for the early symptoms of laryngeal affection, and to be ready to carry into immediate action any course of treatment that appears to be called for. In all cases of laryngeal diphtheria it is absolutely necessary to have instruments ready for operation by the bedside, and this holds good whether the individual practitioner prefers the operation of tracheotomy or the employment of intubation. All cases of laryngeal diphtheria require the same hygienic treatment that is necessary in pharyngeal diphtheria, but when laryngeal symptoms are developing the employment of pure, warm, somewhat moist air is more necessary than in pharyngeal diphtheria. In dealing with children it is essential to employ a well-ventilated tent in which the air is impregnated with steam. Sometimes advantage appears to arise from the use of medicated steam; oil of turpentine has been recommended, a tablespoonful being added to the kettle every two or three hours, and oil of eucalyptus has also been used. For moist disinfectant vapour we use at the Evelina a mixture of creosote and carbolic acid; an ounce of creosote and two drachms of powdered acacia are rubbed together and added to two ounces of solution of carbolic acid (1 in 20), and the mixture is then put into a bronchitis kettle with a pint of water. Sometimes we have employed with apparent advantage the vapour derived from a drachm of terebene to half a gallon of water; but these vapours, although soothing, do not appear to have any specific disinfectant powers. As Dr. Gee has pointed out, no direct specific treatment is possible when dealing with laryngeal diphtheria, since it is obviously impracticable to employ strong disinfectants locally to the larynx, and any attempt to impregnate the atmosphere with disinfectants will be likely to render the air irrespirable. As in cases of pharyngeal diphtheria, much relief may often be obtained from the use of ice or ice-cold applications to the neck, but it will frequently be found that difficulty will be experienced in persuading the friends of the patient to carry out this line of treatment, owing to the dread of increasing laryngitis by the local application of cold. Still, when it can be employed continuously, marked relief frequently results.

If the laryngeal diphtheria is consecutive to an affection of the nose or the pharynx, local applications may be employed, but it must be distinctly remembered that they are being used for the nasal and pharyngeal affections, and that they will be inoperative in checking the disease within the larynx. Hence, so soon as the nasal passages and the pharynx appear to be free of membrane, local applications may be discontinued.

Many practitioners are in favour of the use of emetics, but there has been considerable difference of opinion as to their value. In the majority of cases they appear to be not only unnecessary but harmful, as so many of the emetics possess a powerful depressant influence, which is undesirable in a disease the chief danger of which arises from asthenia. Emetics have been recommended with a view of favouring the expectoration of membrane if, as sometimes happens, the disease has commenced in the trachea and bronchi before the development of laryngeal symptoms. It is, however, extremely difficult in any given case to feel certain that the trachea is involved without affection of the larynx. In the large majority of cases the larynx is affected before the extension of the disease to the trachea and bronchi. The emetic that has received most favour is ipecacuanha, and it is recommended that it should be employed early, and that for a child of from one to five years of age drachm doses of ipecacuanha wine should be administered frequently until vomiting results. Those who advocate the employment of emetics claim that they not only favour the expectoration of membrane, but that they are also serviceable in diminishing the reflex excitability and laryngeal spasm which cause the more urgent symptoms of this disease. It must be remembered that the attacks of dyspnœa occur with periodical exacerbations, and that therefore they are largely due to spasm of the glottis rather than to its occlusion by the development of membrane. Hence any drug which will diminish spasm possesses a theoretical value, and chloral and ipecacuanha have therefore been employed to allay cough and spasm. In some severe cases the use of chloroform has been recommended with the same object, and all who have witnessed the administration of this anæsthetic, previous to operations on the trachea, must have seen the relief of symptoms under its influence.

The internal remedies employed in the treatment of laryngeal diphtheria do not differ materially from those used for pharyngeal diphtheria. Perchloride of mercury has been much recommended, but the tincture of the perchloride of iron seems to give more general satisfaction.

In most cases of laryngeal diphtheria, however, there is very little opportunity for discussing the use of internal remedies. Local treatment by ice and the employment of medicated steam usually form the sole measures which can be adopted before the question of operation arises. In every case of laryngeal diphtheria it is necessary to watch closely for signs of obstruction to respiration, and to act promptly, so as to relieve all mechanical obstruction as early as possible. The earlier surgical interference is made the greater is the chance of ultimate success, and although temporary relief may result from operating even at the latest stages of the disease, if the operation has been delayed until the breathing is stridulous, the muscles of forced respiration in action, and the lips cyanotic, the immediate relief afforded is not likely to avert the impending fatal termination.

It is perfectly obvious that some operative interference is called for in any case of obstructive dyspnœa, and it is therefore well to group once more the symptoms indicative of this condition. The main symptoms are suppression of the voice, depression of the suprasternal and supra-clavicular spaces, sucking in of the lower part of the chest, restlessness and sleeplessness; but although these symptoms urgently call for operation, much discussion has been raised both concerning the mode of relief which it is advisable to use and also concerning the time at which operation should be performed. The two measures which have been recommended are tracheotomy and intubation, and if these two measures have to be considered by themselves without reference to any other mode of treatment, there seems little doubt that the arguments in favour of tracheotomy have the greater weight. The whole aspect of treatment has been very materially modified by the introduction of antitoxin, but it may be well here to compare the two operations regardless of antitoxin. Sterne has summarised the circumstances which are helpful in determining the choice of operation in the following words :—' (1) All things being equal, I would always intubate when the patient is under three and a half years of age. (2) Between the ages of three and a half and five years I would be regulated, of course, by individual circumstances, with the preference for tracheotomy. (3) Over five years of age I would prefer tracheotomy. (4) In adults I would never tracheotomise, but willingly test intubation. (5) Amongst poor people, irrespective of age, I would always intubate. While it sounds harsh to draw such close distinctions, good reasons are forthcoming. The general results of intubation are about equal to those of tracheotomy : skilled attendance, such as is always required after tracheotomy, can only be procured for considerable purchase power, and is in consequence only available where people have means ; while the operator himself may be willing to give his own valuable time, he may owe to other patients attendance that may be of as much value to them as to the child operated upon. (6) Intubation should never be performed at any age where there is a strong probability that the trachea is crowded with membrane. (7) Where skilled attendants cannot be obtained intubation should always be practised.'

The chief argument against intubation is, perhaps, that urged by Dr. Gee—namely, the difficulty of being certain that the disease is confined to the larynx or to the parts above. If the disease has already extended to the trachea, the operation of intubation is less likely to give good results, and sometimes the detachment of membrane from the trachea or from the bronchi may occlude the tube. It is certainly more difficult under these circumstances to remove and reintroduce the intubation tube than to cleanse and replace a tracheotomy tube ; the former requires the presence of a medical man or of a skilled assistant, while the latter may be entrusted to a trained nurse. Although the results of intubation and of tracheotomy appear to be fairly equal it must be remembered that most cases of intubation have hitherto been performed in hospital practice where skilled assistants are constantly available. Whichever operation is performed, there will probably be some difficulty in feeding, a difficulty which must be overcome by the use of the nasal tube. An argument in favour of intubation is that the parents give their consent more readily. There is an instinctive dread of the operation of tracheotomy, and it is, therefore, often postponed in deference to the wishes of friends until it is too late to give any permanent relief. In cases where the disease has not extended to the trachea, intubation is preferable, because the tube does not require changing so frequently, whereas after tracheotomy a good deal of inflammation is excited in the trachea and bronchi, and much mucous discharge results, independently of the expectoration of membrane. Hitherto one of the chief arguments against the early performance of tracheotomy has been the high rate of mortality. Dr. Goodhart considers that the operation in itself adds another risk, and he advocates the postponement of the operation of opening the windpipe to the latest practicable moment, on account of the high mortality. In the Report of the Metropolitan Asylums Board the following table of mortality after tracheotomy occurs :—

Ages	1894		
	Cases	Deaths	Mortality per cent.
Under 1	5	4	80·0
1 to 2	33	29	87·8
2 ,, 3	46	35	76·0
3 ,, 4	53	33	62·2
4 ,, 5	45	32	71·1
5 ,, 10	75	47	62·6
10 ,, 15	1	1	100·0
15 and upwards . .	3	3	100·0
Total .	261	184	70·4

The above figures sufficiently indicate the serious nature of the operative proceedings in connection with laryngeal diphtheria, and the percentage corresponds closely with that which has occurred in my practice at the Evelina in some epidemics. Dr. Goodhart maintains that *in diphtheria* the operation is in itself a serious one, and he bases this statement upon the diffuse inflammation of the cellular tissue of the neck which often follows the operation, and upon the unhealthy appearance of the edges of the wound, which gape and often present a large sloughing surface, which becomes dry and fœtid, and is occasionally even covered with membrane. He argues moreover that another result of the operation may be injury to the mucous membrane and the trachea, and he states that he believes the bronchial pneumonia, the purulent bronchitis, and the excessive tracheitis so often seen in fatal cases of diphtheria are chargeable quite as much to the operation as to the original disease. He refers also to the amount of muco-purulent discharge that is ejected from the tube even in cases that do well, and also to the slowness with which this discharge ceases. One case which occurred in my practice at the Evelina in 1889 may be quoted to illustrate these observations. A child, William R., aged two years and ten months, was admitted on January 24 with urgent dyspnœa, sucking in of the chest wall, and blue lips; patches of membrane were seen on the fauces and the tonsils. There was some alteration of resonance on the left side of the chest behind. The history given was that a week before admission the child was hoarse and had some cough; four days before admission he had difficulty in breathing and sickness. He was restless for two or three days, especially when in bed, and his breathing had been very bad at night. Owing to the urgency of the symptoms tracheotomy was immediately performed, and the temperature rose in six hours to 103°.

After the operation he was very restless through the night, and his neck was swollen. On the 25th the tube became stopped up and the child ceased breathing and became very blue and collapsed. The tube was removed, artificial respiration was performed, and half an ounce of brandy was administered by the rectum, and under these measures he soon recovered. On the 26th he was very restless, throwing his arms and legs about, and a small piece of membrane was removed from the tube; cough was not very frequent, but was very severe. Numerous small patches were seen on the tonsils, which bled readily if touched. On the 28th a large piece of membrane was coughed out of the tube, and several smaller pieces came away during the night, but in spite of this there was still very much sucking in of the chest wall. On the 31st some milk was coughed up through the tube, and although an effort was made to leave out the tracheal tube for a short time it speedily had to be reinserted, as the child became blue and distressed. Much mucus and many small shreds of membrane continued to be expelled from this time until February 27. On March 14 the tracheal wound was enlarged and the larynx was examined, but nothing abnormal was seen. Although many efforts were made to dispense with the tube, on every occasion the child got frightened and distressed and the tube had to be replaced, and it was not until March 20 that the tube was finally omitted, and not until the 27th that the tracheal wound completely closed. The child was discharged in a satisfactory condition on April 1.

In this case doubtless the difficulty of removing the tube mainly resulted from dread, but the case is mentioned here as illustrating well the lengthened course which was occasionally met with prior to the introduction of antitoxin. Dr. Goodhart urges that the only excuse for early performance of tracheotomy is to admit of more thorough application of local remedies to the larynx; but my present practice is to recommend the performance of tracheotomy or intubation so soon as a diagnosis of laryngeal diphtheria has been made, especially if the antitoxic serum can be employed simultaneously.

The selection of operation is largely a matter of individual preference, but my feeling is that if intubation is performed early and antitoxic serum is injected at the same time, there is less likelihood of the membrane extending down the trachea, and portions of membrane which are already formed detach and soften more easily; in fact, the antitoxic serum has robbed the operation of tracheotomy of many of its terrors, as can be seen from the following table of mortality from the Metropolitan Asylums Board during the 'antitoxin year' in cases in which tracheotomy had been performed:—

Ages	1895 (Antitoxin year)		
	Cases	Deaths	Mortality per cent.
Under 1	4	3	75·0
1 to 2	53	36	67·9
2 " 3	38	16	42·1
3 " 4	59	29	49·1
4 " 5	42	18	42·8
5 " 10	57	21	36·8
10 " 15	2	2	100·0
15 and upwards . .	—	—	
Total .	255	125	49·4

Comparing this table with that given previously on p. 92, it will be seen that the total mortality has been reduced from 70·4 to 49·4, and the numbers upon which these percentages are based are practically the same. Although this table tells in favour of tracheotomy we have more recently at the Evelina obtained similar improved results from the performance of intubation, and in fact the operation of tracheotomy is now rarely performed in our practice. It is true that the use of intubation necessitates constant watchful care both on the part of the nurse and on the part of the resident medical officer, since the risks of obstruction to the tube can never be lost sight of, but hitherto we have had no bad results from blockage of the intubation tube.

If the operation of tracheotomy is deferred too late, although it relieves some of the laryngeal dyspnœa it will be found that the relief obtained is not complete. Frequently much lividity persists, the improvement in colour is only partial, and at a later stage pulmonary changes develop and lead to the fatal termination. Very commonly after the operation of tracheotomy some rise of temperature is to be expected. In the case already referred to, it will be seen that although the natural tendency of diphtheria is to be associated with a low temperature, yet the temperature rose to 103° shortly after the operation. Such rise of temperature may sometimes be due to the development of pulmonary complications, but the rapidity with which it occurs mostly precludes this explanation.

When the operation of tracheotomy has been performed it is well to remove the tube as early as possible. Efforts should be made to dispense with it in twenty-four hours if possible, for it must be remembered that the tube is in itself a source of irritation, and that its continued presence is likely to lead to inflammatory changes, both locally and in the pulmonary tissue. If the tube is kept in too long there is likely to be difficulty from granulations of the wound, and troublesome cicatrices are likely to form; in fact, on every ground the advantages of the operation must be regarded as limited to the immediate relief of symptoms. Sometimes, especially in cases where the tube has been kept in too long, considerable difficulty is experienced in its final removal.

Occasionally the difficulty seems to result from paralysis of the muscles of the larynx, so that the glottis is closed instead of opened during efforts of inspiration. This form of paralysis is stated to be most common in cases in which the operation of tracheotomy has been performed, but it occasionally occurs as part of the general paralysis of the pharyngeal and laryngeal muscles consecutive to diphtheria. More often the difficulty of removing the tracheal tube results from dread; the child, having been accustomed to the relief of breathing afforded by the presence of the tube, voluntarily ceases breathing when the tube is removed. In the case of the child referred to on p. 94, this was doubtless the chief reason for the length of time which elapsed between the operation and the date at which the tube was finally removed; although in that case the possibility of laryngeal paralysis was at one time favoured by the return of fluids through the tracheotomy tube.

It is not at all uncommon to find children who can breathe perfectly through the larynx when the tracheotomy tube is plugged, but who show great excitement and develop symptoms of dyspnœa so soon as the tracheotomy tube has been removed. Children appear to become accustomed to the presence of the tube, and frequently breathe in an irregular fashion and become nervous and excitable when the tube is removed. The excitement in such cases appears to induce spasm of the glottis.

Intubation of the larynx.—The future treatment of diphtheria appears so likely to necessitate the more frequent use of intubation, that it is deemed advisable to consider this operation at some length.

The operation was originally advised by Bouchut, of Paris. in 1858, although others had previously recommended the introduction of a metallic tube into the larynx for the relief of dyspnœa, independently of diphtheria. The results obtained by Bouchut were so far from satisfactory that the procedure fell into disuse until it was revived by Dr. O'Dwyer, of New York, in 1880. To his advocacy and to his modifications of the tube the present method of operating is due, and it will perhaps be best to describe the operation and the instruments in his own words :—

'**The instruments.**—A set of intubation instruments consists of six tubes, each supplied with a separate obturator, an introducer, extractor, mouth-gag, and a scale. The obturator when in position projects a little beyond the lower extremity of the tube, and is rounded off into a probe point to prevent pushing down pseudo-membrane and injuring the tissues of the larynx. It also serves as a means of attachment to the introducer. The numbers on the scale indicate the years for which the corresponding tubes are suitable. The smallest tube when applied to the scale will reach the first line, marked 1, and is suitable for children of one year and under. This tube can be used with children of two

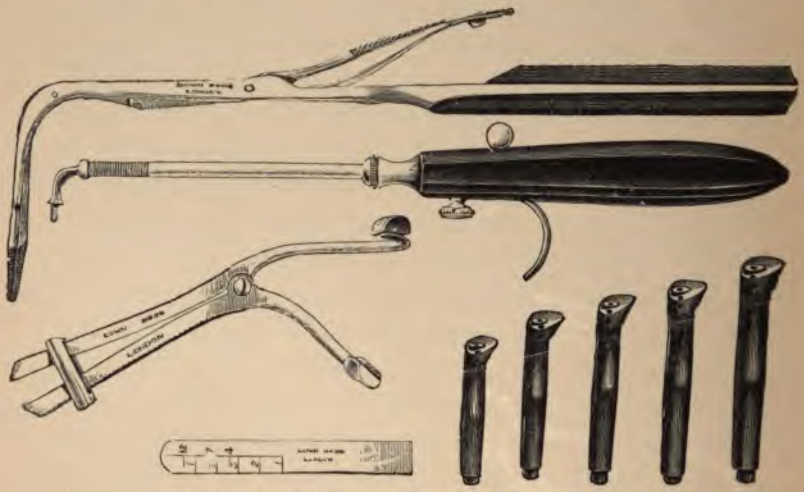

Fig. 9.—Dr. O'Dwyer's Intubation Instruments

years with perfect safety, as far as slipping into the trachea is concerned, but the probability of its being coughed out would be great. The second size reaches the line marked 2, and is suitable for children between one and two years old.

'The third size is for children between two and four years old, and the next size for children from four to seven years old. The next size, reaching the line marked 8–12 on the scale, is for children up to twelve years of age, but not after puberty, as the sudden increase in the size of the larynx at this time would render it liable to pass through into the trachea. The largest size is intended for those children whose larynx is so large that the No. 5 tube is not retained.

'The female larynx in children, as in adults, is smaller than the male, which should be taken into consideration in selecting the tube, as well as the size of the child compared with its age. For instance, in a small delicate girl of four years a No. 2 tube would be the proper one; while, on the other hand, in some boys of three and a half years it would be advisable to use the 5–7 size, especially if the case is a considerable distance from you, and coughing out the tube would entail some danger and a great deal of inconvenience.

'When the proper tube is selected for the case a fine thread of braided silk is passed through the small hole near its anterior angle, and left long enough to hang out of the mouth, its object being to remove the tube should it be found to have passed into the œsophagus. The obturator is then screwed tightly to the introducer and passed into the tube. It is well to push off the tube once or twice before using it, to see that everything works smoothly.

'**Method of introducing the tube.**—The following is the method of introducing the tube, which is done without the use of an anæsthetic: The child is held upright in the arms of the nurse, with its head on her left shoulder, to avoid interfering with the mouth-gag, and the arms are secured to the sides, either by being held below the elbows by the nurse or by wrapping a sheet around the body. The legs should be secured between the nurse's knees. The gag is inserted in the left angle of the mouth, well back between the teeth, and opened as widely as possible without using undue force. An assistant holds the head, thrown somewhat backward, while the operator inserts the index finger of the left hand to elevate the epiglottis and direct the tube into the larynx. The instruments should be worked in the median line, the operator facing the patient squarely. The handle of the introducer is held close to the patient's chest in the beginning of the operation, and rapidly elevated as the tube approaches the glottis. Very little force is necessary to overcome the obstruction, and if the tube does not enter the larynx easily, it should be withdrawn and another attempt made. It should be pushed well down into the larynx before it is detached from the obturator; and while removing the obturator it is necessary to keep the finger in contact with the head of the tube, to prevent it being also withdrawn. The string should not be removed until the dyspnœa is relieved and the operator is certain that the tube is in the larynx. In some cases the string causes so very slight an amount of irritation that I allow it to remain for ten or fifteen minutes, to excite more cough and thus expel the accumulated secretion and overcome any collapse of the lung that may exist. When the thread is withdrawn the finger must be kept in contact with the tube to prevent its being also withdrawn. In removing the tube the child is held in the same position, but the head is not thrown quite as far back. The finger which is used as a guide for the extractor is brought in contact with the head of the tube, and then pressed toward the patient's right, in order to uncover the aperture and allow the extractor to enter in a straight line. Continuous pressure with the thumb is made on the lever above the handle while the tube is being withdrawn.

'Owing to the small aperture of the tube compared with the size of the larynx, the extraction of the tube is more difficult than its insertion. It is during this part of the operation that the greatest amount of injury is liable to be done to the larynx by pushing the instrument down outside the tube and removing it forcibly with the blades widely open. It requires no force whatever to remove a tube from the larynx, and if any resistance is felt, it will be found that the point of the extractor is not in the tube, but caught in the surrounding tissues. To reduce this danger as much as possible, I have added a regulating screw which prevents the blades from opening wider than is necessary to hold the tube firmly. It can be adjusted to suit a tube of any size.

'What are the evidences of the tube being in the larynx? The first thing noticed is that cough sets in which has a decidedly tubal character, and once heard is not readily forgotten. The more or less cyanotic condition usually disappears, and the child becomes more quiet. When the tube has been passed into the œsophagus instead of the larynx, this is known by the string which is attached to the tube becoming gradually shorter, by the absence of much spasmodic cough, and the non-relief to the dyspnœa.

'Being satisfied that the tube is in the larynx, and that the condition of the child is satisfactory, the string may be removed, and the next step is the careful feeding of the patient. To avoid the tendency of food finding its way into the larynx, it is well to adopt Waxham's plan of feeding young children under such circumstances; and that is to so place the child that its head is lower than its feet, fluid food being administered by means of an ordinary feeding-bottle to which a rubber nipple is attached. To alleviate thirst, Waxham recommends cracked ice and ice cream. Stimulants should under these circumstances be administered only by enemata.

'The proper time for removing the tube from the larynx will depend upon the age of the patient, the character of the disease, whether of slow or rapid development, and the progress of the case. The younger the patient, as a rule the longer the tube will be required. In children under two years it is better to leave it in for seven days. When the disease has developed slowly, and has therefore run a greater part of its course before calling for operative interference, the tube can be dispensed with earlier, sometimes as soon as the second or third day. If the case be at such a distance as to render it impossible to reach it in a reasonable time, it is safer, if progressing favourably, to leave the tube in position for seven or eight days, and the exceptions are few in which it will be necessary to reinsert it after this time. The tube should always be removed on the recurrence of severe dyspnœa, because it is sometimes impossible to ascertain with certainty whether it be partially obstructed or not. The best evidence to the contrary is a good respiratory murmur or numerous râles over the lower portion of the lungs. The development of a high temperature, especially if accompanied with any considerable amount of bronchitis on the third or fourth day, is a sufficient reason for removing the canula, as it can sometimes be permanently dispensed with as early as this; and even if left out only for a few hours without urgent dyspnœa, is of great benefit, as it affords an opportunity to unload the bronchi of secretions by permitting complete closure of the glottis, and thus giving full effect to the act of coughing.

'In those cases which refuse nourishment after intubation, or that cannot be induced to take a sufficient quantity, it is useless to remove the tube for the purpose of feeding unless it has been in long enough to give some reasonable hope that its further use will not be necessary, as it is difficult to convince children for some time that they can swallow any better than before. If no dyspnœa recurs in half an hour after the extraction of the tube, it is safe to leave the patient if not at too great a distance to be reached within two or three hours.'

The cases of diphtheria which are favourable for intubation are those where the obstruction comes on rapidly, and where the dyspnœa is due to œdema of the mucous membrane of the larynx, or to spasm rather than to the extensive formation of membrane; on the other hand, if there is much swelling of the tonsils and fauces, and if also the dyspnœa has developed more slowly, the operation is less likely to be successful, and in such cases a resort to tracheotomy may be necessary. Still, there is no harm in endeavouring to avoid the more formidable operation by the use of intubation, since the operation is in itself fairly free from danger, and it is one for which the consent of the parents may be readily obtained, and it does not interfere with the chances of a successful result upon a resort to tracheotomy at a later stage.

Diphtheria treated with intubation and antitoxin.—Thomas N——, aged six years and ten months. Admitted June 9, 1896. Taken ill on the previous day with cough and pain in chest; cough sounded to the mother like croup. On admission breathing very difficult. Child put into a hot bath at once and drachm doses of ipecacuanha wine given every ten minutes until the child was sick, five such doses requiring to be administered. The lower ribs were much drawn in during respiration; no loss of resonance was detected over the lungs, and the lung sounds appeared to be normal. No membrane could be seen on tonsils or soft palate; pulse intermittent; frequent sickness. Breathing became worse three hours after admission, and intubation was performed, after which the face and lips regained colour, and the breathing became easy. A small piece of membrane was expectorated on the 11th, and for the first time a small quantity of albumen was found in the urine. The tube was taken out on the 11th, and 4 c.c. of antitoxin injected. From this time the child progressed favourably, the temperature remaining near the normal, and on the 16th the child was able to sit up (fig. 10).

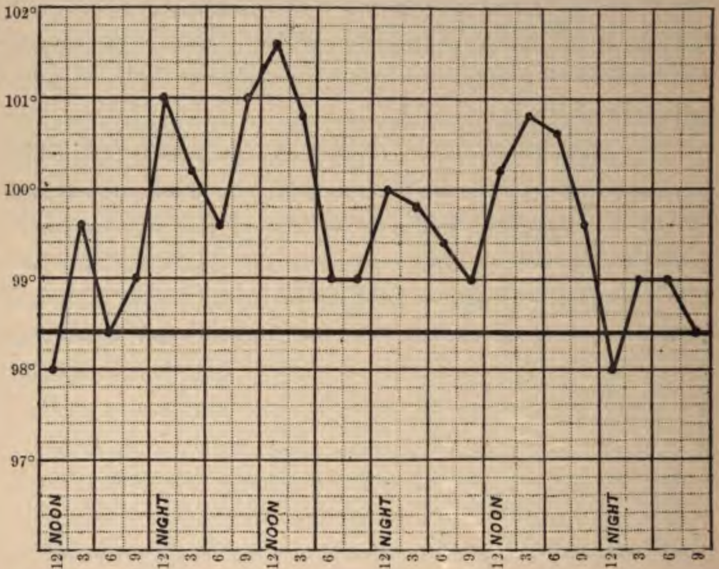

Fig. 10.—T. N., aged 6 years 10 months. Admitted June 9, 1896. Intubation at 7 p.m. on day of admission; tube removed on June 11 and antitoxin injected

Reference has previously been made to the possibility of detaching a mass of membrane below the intubation tube, and of the possibility of occlusion of the tube by this means; but such an accident, although possible, appears rarely to occur, and almost invariably leads to violent respiratory efforts, during which both tube and membrane are apt to be forced out of the larynx. If, however, this should not follow during the temporary arrest of respiration the tube must at once be withdrawn. Sometimes, when too small a tube has been used, it may be coughed up or drawn down by the inspiratory efforts, and in such a case a larger tube must be tried. Cases are recorded in which the intubation tube has been coughed up and swallowed, but no fatal results have, so far as I know, followed from this accident. Cases of intubation require the utmost watchfulness on the part of the nurse, and she must be instructed to withdraw the tube should dyspnœa suddenly develop. This is usually performed with ease by traction on the thread, but Dr. Wharton, of Philadelphia, refers to a case in which the thread having been withdrawn, it was found possible to dislodge the tube by inversion of the child and by striking over the posterior portion of the chest.

The tube is usually retained in its place until the swelling of the laryngeal tissues subsides, and is then easily dislodged by an effort of coughing. This may be expected at any time after the end of the second day ; but if it has not occurred, the tube may be mostly dispensed with at the end of three or four days. Sometimes, as when removing the tracheotomy tube, urgent dyspnœa immediately follows, and it is then necessary to replace the tube promptly. The intubation tube, whenever removed, should be thoroughly cleansed and boiled so as to sterilise it for subsequent use. The removal of the tube may sometimes, as O'Dwyer points out, be postponed for seven or eight days, and if it cannot be readily detached by traction, a mouth-gag and the extractor must be used.

The whole operation of intubation is one which requires careful manipulation and an accurate knowledge of the relations of the larynx. If by any mischance the tube has been passed into the œsophagus instead of through the glottis, no efforts of coughing result, and no relief to the breathing is afforded; the usual immediate result of the proper introduction of the tube is violent coughing, which is speedily followed by relief to respiration.

Many have dwelt on the difficulties of feeding satisfactorily after the employment of intubation. The epiglottis appears to be interfered with, and liquids passed into the pharynx may occasionally find their way into the larynx. Many ways of overcoming this difficulty have been suggested. When it is necessary to feed with liquids, it has been stated that children can swallow well if fed from a nursing bottle, the head being dropped over the nurse's knee so as to be lower than the body. This expedient we have rarely found necessary, as in nearly all cases where intubation has been performed we have fed for the first few days by means of a flexible tube passed down the nose into the œsophagus. The employment of the nasal tube in diphtheria is frequently facilitated by diminution of the sensibility of the larynx. This, however, may favour the passage of fluids into the trachea, and it has been urged that considerable care should be taken in passing the nasal tube from the dread of flooding the trachea and bronchi. I consider however that it is really rather a difficult thing to pass the nasal tube into the larynx, and this is practically impossible when the chink of the glottis is already occupied by the intubation tube. It has been recommended that if children are unable to take liquid nourishment at the first, success may attend the use of a diet which is semi-solid, but in these cases complaint is likely to be made of thirst, and it may be necessary to supply liquids, either by enemata of water or by giving ice to suck.

Tracheotomy in diphtheria.—The indications for tracheotomy in diphtheria are similar to the needs of intubation, and although it will have been seen that I consider this operation less frequently called for now than previous to the introduction of antitoxin, cases frequently arise in which the practitioner has really no choice. The intubation instruments may not be at hand, and the urgency of the symptoms may demand immediate relief; and it may sometimes be necessary to perform tracheotomy after intubation has been attempted unsuccessfully. Reference has previously been made to the reduction in the mortality after tracheotomy which has resulted from the employment of antitoxin, but notwithstanding this improvement, the operation of tracheotomy is still one which has a high death-rate, and it is therefore one which is only performed as a matter of necessity. If, however, the laryngeal dyspnœa is urgent, the operation is one which must be performed speedily before allowing the child to pass into a condition of hopeless toxæmia.

Tracheotomy : death from asthenia.—Edward J. B——, aged three years. Brought to the hospital with the following history: Quite well until three days before admission, then coughed 'like the croup ;' became worse, and had difficulty of breathing, especially at night. Was very restless and feverish. On admission breathing much distressed, sucking in, face blue; temperature 100·8° Tracheotomy was at once performed under chloroform. Breathing much easier, face very flushed ; temperature first rose to 101°, then fell to 100°, and rose again to 103°. Slept at short intervals ; very restless at times, throwing limbs about ; breathing became very distressed, face blue and limbs quite rigid ; a good-sized piece of membrane was coughed up ; cough frequent, dry, not severe ; extremities cold. Hot-water bottles were applied. On the following morning the child was much weaker, face very blue, breathing rapid and distressed, was also slightly sick twice ; at midday he became convulsed, hands and feet cold, breathing very much distressed, and he died within half an hour of the convulsion.

Tracheotomy : paralysis of diaphragm ; death with pneumonia.—Eliza D. J——, aged two and a half years. Admitted October 25, 1893. Eight days before seemed ill and refused solid food. The night before admission breathing got much worse. On admission there was considerable retraction of suprasternal and supraclavicular spaces, also of epigastric angle and lower intercostal spaces, but not much cyanosis. Loud laryngeal stridor masking vesicular murmur over chest wall; temperature 101·2°; pulse 140; respiration 44; fauces much swollen and very red; diphtheritic membrane on both tonsils and on base of uvula. Was fairly comfortable for five hours after admission, the stridor decreasing, then the child suddenly became more cyanosed and stopped breathing. Tracheotomy was performed at once and gave relief. No membrane seen at the time of the operation. On the 26th coughed up a little membrane; albumen found in urine. On the 27th temperature subnormal; a large cast showing bifurcation of trachea removed through the tube wound. Cough rather frequent and troublesome; sick. On the 28th fed by nasal tube; still coughing up membrane; pulse a little quicker, but full and regular. On the 29th the outer tube left out for four hours, but the wound closing over the tracheal opening, the child got blue and the tube had to be replaced. On the 30th tube again left out for a short time, but had to be replaced; small pieces of membrane still being coughed up. On the 31st fed by the mouth; cough less troublesome; the tube left out; fauces much cleaner. November 1: Tube still out; hardly any membrane visible on the fauces; she is able to breathe through the mouth, and always does so when asleep. On the 3rd tracheal wound filled with a strip of iodoform gauze; pulse not quite so good, more frequent, ranging from 148 to 156. On the 6th first noticed not to be using its diaphragm much; urine still contained albumen. On the 7th paralysis of diaphragm more marked; child made no attempt to speak; respiration rather quicker; very restless and blue after feeding. On the 9th the child died, both pulse and respiration failing; no convulsions.

Post mortem.—The aryteno-epiglottidean folds very much thickened and swollen; all tissues in the larynx seemed infiltrated; glands between trachea and œsophagus enlarged; lining of bronchi much injected; bronchial glands swollen; bronchial pneumonia of the right upper lobe, left lower lobe completely solid; kidneys very congested; renal veins much enlarged.

The operation of tracheotomy is so well described in numerous text-books of surgery that it is unnecessary to enter into any detail here. It is well, however, to point out that, notwithstanding the urgency of the symptoms calling for the operation, the employment of an anæsthetic is always advisable, and to indicate that the choice of the anæsthetic is a matter of considerable importance. Ether should always be avoided, not only because the operation so often has to be performed by artificial light, and there is therefore danger of ignition of the vapour, but also because ether provokes laryngeal spasm and promotes the formation of mucus within the air passages; on the other hand, chloroform allays spasm of the glottis and therefore renders the breathing more easy, even in the most urgent cases. Very commonly after the trachea has been opened respiration ceases suddenly, and although this accident has sometimes been attributed to free bleeding, I have witnessed it where the bleeding has been quite under control, and in such cases inversion and artificial respiration must be at once performed. In one such case which I witnessed recently artificial respiration had to be continued many minutes before the normal rhythm was resumed. Sometimes this arrest of respiration has appeared to be due to the irritation of the interior of the trachea in endeavours to clear out portions of membrane before inserting the tracheotomy tube, and it is as a rule better to avoid irritating the trachea in this way. If blood, mucus, and membrane come away freely from the wound, they should of course be removed, but it is undesirable to attempt to dislodge portions of membrane which may be seen attached to the interior of the trachea. Usually, immediately after the operation, the relief afforded is most satisfactory: respiration becomes quiet and even, the lividity of the lips and face passes off, the normal colour is regained, and it is by no means unusual for the child to pass into a quiet sleep very speedily.

Tracheotomy, with immediate relief; pulse intermittent; albuminuria.– Fred P——, aged three and a half years. Admitted October 17, 1895. Breathing stridulous; loud croupy cough; sucking in of lower part of chest and of lower part of neck; tonsils slightly enlarged; no exudation visible; glands at angle of jaw rather large; very little air entering the chest; temperature 98·2°; pulse 98; respiration 60; no albumen in urine. The breathing increasing in difficulty, tracheotomy was performed, which gave much relief, although no membrane was seen during the operation. On the following day the temperature rose to 103°, the pulse to 158, but in other respects the child seemed comfortable. On the 19th small pieces of membrane were expectorated; urine contained a trace of albumen. During the night of the 20th breathing became laboured and pulse almost imperceptible; expectoration slightly tinged with blood; cough frequent and severe. Membrane stained with Loeffler's stain showed diphtheritic bacilli. On the 21st tube left out all day; pulse irregular and intermittent. From this time the child convalesced rapidly, although the pulse remained intermittent until November 12.

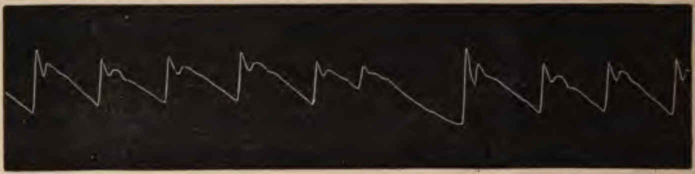

FIG. 11.—FREDERICK P., AGED 3½ YEARS, SEVEN WEEKS AFTER TRACHEOTOMY FOR DIPHTHERIA

The success of the operation of tracheotomy is to a large extent dependent upon the nurse, and it is therefore most necessary for the child to be under the care of a nurse who has had experience in similar cases, and who is ready to deal with any emergency that may arise. The need of a tent and of a bronchitis kettle after tracheotomy has already been mentioned. Some recommend the employment of various sprays in the after-treatment of cases in which tracheotomy has been performed; hand sprays or steam sprays have been used, and various solutions have in this way been applied to the larynx; for example, peroxide of hydrogen, carbonate of sodium, or dilute carbolic acid. In our practice at the Evelina, since the introduction of antitoxin we have entirely discarded local applications. The membrane appears to detach so speedily and easily after the use of antitoxin that local treatment is unnecessary, and as it causes disturbance of the patient it is unwise. The direct application of various solutions through the tube by means of a feather we have also entirely given up. These seem to irritate the trachea and to possess no compensating advantage. It is essential to use a double canula, so that the inner tube can be freely removed for the purpose of cleansing. This removal of the inner tube is requisite every hour or so for the first twenty-four hours; and the inner tube after being thoroughly cleansed should always be replaced speedily, otherwise the outer tube is liable to become blocked or uneven from an accumulation of mucus, and the return of the inner tube can only be effected with difficulty. If portions of membrane are seen in the interior of the inner tube they may be removed with a feather, or with a small pair of forceps, but as a rule the less the trachea is interfered with the better. Prior to the introduction of antitoxin the final removal of the tube was frequently a matter of difficulty. It was recommended that it should be removed on the third or fourth day and replaced by a fresh one, which should be left *in situ* for two or three days more. There can be no doubt, however, that the date of the permanent removal of the tracheotomy tube has been considerably advanced since the introduction of the antitoxin serum. Dr. Wharton states that he has seen tubes removed permanently as early as the third and as late as the sixtieth day, and he thinks that usually the tube can be removed permanently from the eighth to the fifteenth day. In most of our cases at the Evelina, since employing antitoxin we have been able to remove the tube at the end of the second day; although previous to this I have had one case in which the tube could only be dispensed with on the fifty-fifth day.

With regard to feeding after tracheotomy, the same precautions are necessary as when intubation has been performed, and it is essential that the most nutritious diet, together with alcohol, should be administered. Should regurgitation of fluids through the wound occur, it will be necessary to feed with the nasal or œsophageal tube; and in most cases it is I think better to feed in this way than to excite the child by constant movements.

Of the complications likely to arise after tracheotomy, the most alarming is perhaps diphtheritic infection of the wound, but this must not be mistaken for the sloughing which is sometimes seen in badly-nourished children. Œdema of the neck sometimes occurs and involves the tissues in the neighbourhood of the wound, while erysipelas is also an occasional sequel. Surgical emphysema in the neighbourhood of the wound is somewhat common, and unless it becomes extreme, the air is usually quickly absorbed. A trouble sometimes arises from the formation of granulations about the tracheal wound, and these necessitate the application of some form of caustic. If the tube is left in for an unduly lengthened period, some tracheitis or ulceration of the trachea may arise, especially if the tube is one which does not fit properly.

Tracheotomy followed by secretion of much tenacious mucus, and by pneumonia.—Charles H——, aged four years and nine months. Admitted October 26, 1893, died November 2, 1893. Taken ill five days before admission with sore throat, and mother thought he was going to have scarlet fever. Brought to hospital with statement that on previous night he had wakened with croup. On admission rather cyanosed; rachitic head; chest well shaped, air entered very badly; much retraction of lower intercostal spaces and epigastric angle; on inspiration all vesicular murmur masked by the loud laryngeal sounds. Considerable swelling of fauces; tonsils enlarged, the right almost covered by diphtheritic membrane, the left had less on the surface: a little membrane could be seen at the base of the uvula. The child was restless, and knee jerks were absent. The cyanosis increasing, tracheotomy was performed on the 27th. Fairly good night; pulse weak at times; no membrane coughed up; short, moist cough very troublesome. On the 28th small pieces of membrane were coughed up and much thick yellow mucus, which readily blocked the inner tube. On the 30th edges of wound very ragged, but no sign of any membrane or cellulitis; small patch of membrane still on right tonsil; child seemed fairly comfortable, but frequent cough disturbed him and prevented sleep. On November 2

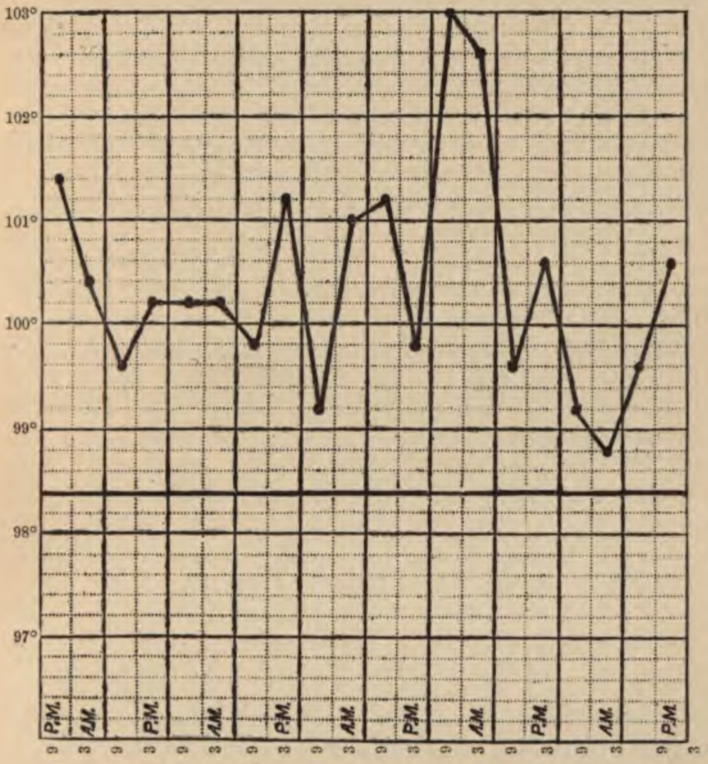

Fig. 12.—Charles H., aged 4 years 9 months. Tracheotomy. Pneumonia

had a convulsion, due apparently to non-oxidation. There was no obstruction in the larynx to be made out. The pulse gradually failed as the respiration became more shallow, apparently in consequence of the child's inability to clear his air passages from the thick tenacious mucus secreted in large quantities. Pulse varied from 120 to 152, consecutive three-hourly records being often from 20 to 30 beats apart. General range of temperature under 101°; only once 103° (see chart). Urine contained albumen from October 30 to the time of death.

Post mortem.—Vocal cords much thickened, œdematous; no membrane; mucous membrane and trachea very red, this redness extending down to the medium-size bronchi; small granular-looking patches of membrane which could be readily separated as far as the first division of the bronchi; one small patch below the tracheotomy wound, where there was a definite loss of substance, possibly produced by pressure from the tube; bronchial glands swollen, one at the lower end of the trachea had suppurated.

Tracheotomy; recovery.—Thomas C. B——, aged four and a half. Admitted February 11, 1889. Dry cough four days; pain in chest; harsh voice; increasing difficulty in breathing. On admission patches of membrane were visible on both tonsils; much cyanosis; breathing distressed; considerable sucking-in of chest wall; temperature 101°. Tracheotomy was performed at once; temperature fell to 99° in six hours; much membrane brought up through tube; occasional profuse general perspiration; breathing mostly easy, although rather distressed at times. On the 14th slightly sick twice; tube taken out on the 17th. On the 18th breathing very croupy. On the 19th small piece of membrane on the wound; knee jerks present. No albumen throughout. Discharged well February 25, 1889.

While laying much stress upon the advisability of the early performance of tracheotomy in cases with signs of laryngeal obstruction it may be well to indicate once more that the introduction of antitoxin has rendered it possible to obtain good results in a large number of such cases by the much milder operation of intubation. I would repeat that if antitoxin has been employed, it is better to try the effect of intubation before resorting to the more formidable operation of tracheotomy.

CHAPTER VII

ANTITOXIC SERUM IN THE TREATMENT OF DIPHTHERIA

The antitoxic serum in the treatment of diphtheria.—Notwithstanding the dangers of forming hasty estimates of the value of new remedies in the treatment of any disease, the time seems to have arrived when it is possible to draw certain conclusions respecting the value of antitoxic serum in the treatment of diphtheria.

It has been very widely employed since its introduction in 1894, and although there have been many who have hesitated to receive the frequently highly coloured pictures of its beneficial results, yet the general consensus of opinion appears to be that in antitoxin, although we do not possess a specific which can be counted upon to save life in all cases, yet a new element has been introduced which has completely altered the clinical features of diphtheria. Sufficient time has now elapsed, and the treatment has been so widely employed and so closely criticised, that it is possible to speak calmly of the good that may be expected to result from the use of antitoxic serum.

In the Report of the Metropolitan Asylums Board the medical superintendents state their conviction that 'in antitoxic serum we possess a remedy of distinctly greater value in the treatment of diphtheria than any other with which we are acquainted,' and these conclusions it must be remembered are drawn from an unbiased consideration of a very large number of cases. It is true that the cases submitted to treatment underwent a certain selection; that the serum was administered only to cases which, at the time when they came under observation, were severe or which threatened to become so; and that no antitoxin was given in a certain number where the patients were moribund at the time of their arrival at the hospital, and appeared therefore to be beyond the reach of any treatment. The valuable Report which has been drawn up indicates that no less than 61·8 per cent. of the admissions were treated with antitoxin, and that noless than 46·4 per cent. of the antitoxin cases were under five years of age. On account of the difficulty of fairly comparing the mortality of those treated with antitoxin (since in children diphtheria is notoriously most fatal) the tables compare the cases which occurred during 1894, when antitoxin was not employed, with those coming under observation in 1895, when a large proportion were treated with serum; and the numbers for the two years, being in both instances over 3,000, are sufficiently large to enable definite deductions to be drawn from them. The conclusions arrived at are so interesting that they may be quoted in full.

It is stated that certain effects have been observed clinically to follow the administration of antitoxin in cases brought under treatment at a reasonably early date. They are: (1) a diminution of the faucial swelling and consequent distress; (2) a lessening, if not an entire cessation, of the irritating and offensive discharge from the nose; (3) a limitation of the extension of membrane; (4) an earlier separation of the exudation; (5) a limitation and earlier separation of membrane in laryngeal cases; (6) an improvement in the general condition and aspect of the patients; (7) a prolongation of life in cases which terminate fatally to an extent not obtained with former methods of treatment. The conclusions from the statistics and clinical observations are summarised as follows :—Improved results in the diphtherial cases treated during the year 1895 are : (1) great reduction in the mortality of cases brought under treatment on the first and second day of illness ; (2) the lowering of the combined general mortality to a point below that of any former year ; (3) the still more remarkable reduction in the mortality of the laryngeal cases ; (4) the clinical improvement in the results of tracheotomy at each separate hospital ; (5) the beneficial effect produced on the clinical course of the disease.

As soon as Behring's antitoxin was obtainable, experiments with it were commenced at the Evelina Hospital. Previous to this our hospital statistics did not compare favourably with those derived from private practice, or even with those of the fever hospitals, because the cases we admitted were necessarily of a very severe type. Until antitoxin was in our possession, however certain our resident officers might feel about the diagnosis of cases of diphtheria brought to them for admission, the general practice was to send away to a fever hospital all cases in which the delay and the journey seemed not likely to be prejudicial, and to admit only those children who presented great urgency of symptoms—in fact, those only in whom it was probable that tracheotomy might shortly be required, even if it was not absolutely essential that it should be performed immediately on admission. As we selected bad cases, our death-rate was necessarily high, and although occasionally our resident officers might boast of having performed many tracheotomies with a large percentage of recoveries, we have arrived at the conclusion that different epidemics varied in the rate of mortality quite as much as different men differ in manual dexterity. Upon the introduction of Behring's antitoxin we determined to employ it, although some of us were somewhat sceptical, since the published results seemed almost too good to be true. I must here gratefully acknowledge the valuable assistance in the management of our antitoxin cases cheerfully given by the nursing staff and the resident medical officers of the Evelina Hospital, especially Dr. Wainwright and Mr. Quennell. We were fortunate in being able to obtain a fairly continuous supply of antitoxin for treatment, and we fitted up a small isolation ward and thenceforward admitted the cases as they came. The early cases were so successful that we were encouraged to continue the treatment.

The first case was so severe that, as the amount of antitoxin then at our disposal was only small, some hesitation was felt about its employment. The case was one of laryngeal diphtheria in which it was necessary to perform tracheotomy immediately, and at the same time 10 c.c. of Behring's No. 2 solution were injected into the muscles of the thigh.

Tracheotomy ; antitoxin ; recovery.—A badly nourished boy, five years of age, was admitted to hospital on November 3, 1894, in an apparently moribund condition, with extreme dyspnœa and only occasional attempts at respiration. Tracheotomy was performed at once, followed by artificial respiration. The respiration became in a short time fairly good, but large quantities of foul-smelling mucus poured from the trachea. Both tonsils were covered with whitish membrane, and there was much offensive nasal discharge. The glands were much enlarged, and there was one-tenth albumen in the urine. The disease was of ten days' duration according to the mother's account. The pulse after operation was 144, the respiration 48, and the temperature 101·6° F. Behring's No. 2 solution (10 c.c.) was injected while tracheotomy was being performed. The pulse remained about 140 for two days and the respiration from about 36 to 40, but there was rapid and marked improvement in the heart sounds. On the afternoon of November 4 the child was well enough to look at a picture book of his own accord. Large quantities of mucus and several pieces of membrane continued to be coughed up, and the temperature remained between 99° and 100°. On

November 6 the throat was quite clean, though still œdematous, the pulse was 120 and full, the respiration 28, and the temperature normal. The tracheotomy tube was removed on the same day, and recovery was quite uneventful, except that a fine trace of albumen remained until the 13th. On the 27th the patient was discharged in excellent condition. (Fig. 13.)

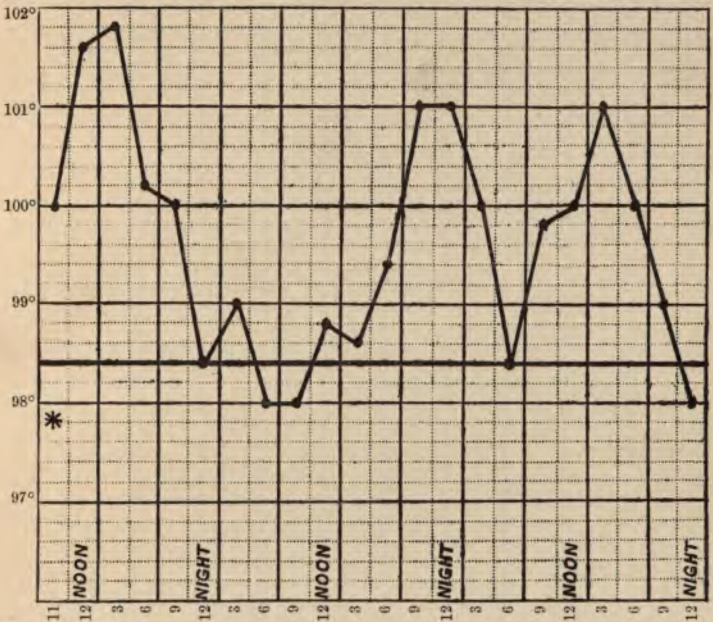

FIG. 13.—W. C., AGED 5 YEARS. ADMITTED NOVEMBER 3, 1894. ANTITOXIN INJECTED AND TRACHEOTOMY PERFORMED ON ADMISSION

This case improved so rapidly that others were treated with a greater degree of confidence. The second case terminated fatally, but this ending was due to a deep ulceration of the tonsils and hæmorrhage from a branch of the right tonsillar artery.

Since then the cases that have been treated at the Evelina have been of all degrees of severity, some requiring tracheotomy immediately on admission, some affecting the tonsil only, others tonsils and uvula, and many affecting the larynx and naso-pharynx; and the outcome of our experience has been to establish a strong case in favour of the antitoxin treatment.

The good effects which we have noted are the rapid detachment of membrane and the great improvement in the general condition of the patient.

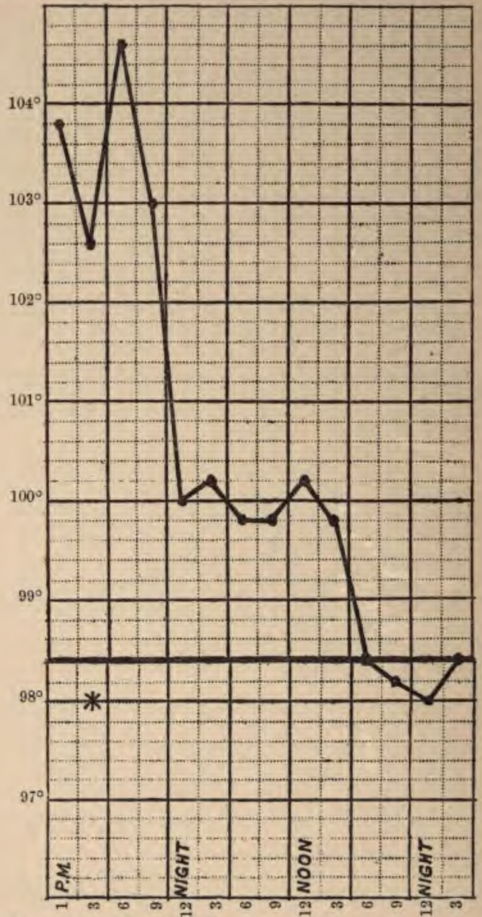

Fig. 14.—Arthur S., 2 years 8 months. Admitted December 17, 1894. Antitoxin injected at 2.15 p.m.*

Both tonsils ; recovery.—Arthur S——, aged two years and eight months, was admitted on December 17, 1894, suffering from an attack of diphtheria of twenty-four hours' duration. On examination he was found to be a well-nourished child. The pulse was 144, small, and compressible, but quite regular; the respiration was 44, deep and easy, with no adventitious sounds in the chest; and the temperature was 104° F. A faint trace of albumen was found in the urine. Both fauces showed well-marked congestion, with, on the right tonsil, a mass of thick, tough, greyish-white membrane about the size of a sixpenny piece, and on the left tonsil there was a smaller but well-defined patch of the same character. Ten cubic centimetres of Behring's No. 1 solution were injected on the patient's admission, and the throat was swabbed and sprayed with a chlorine water gargle. Nine hours afterwards the pulse was 132, fuller, and less compressible, the respiration 32, and the temperature 100°. He slept well during the night and did not complain of any tenderness when swallowing. The following morning the pulse was 120, the respiration 26, and the temperature 99°. The child was looking bright and happy. The membrane on the throat had not spread, and was becoming detached on the edges and of a greyish colour. The same night the pulse had fallen to 100, being good and full. The temperature was normal and the respiration 24, the general condition being excellent. The albumen had disappeared from the urine. Patches were still to be seen on the tonsils, but were rapidly disappearing. Twenty-four hours later the pulse was good, varying between 100 and 110, the respiration 24, and the temperature still normal. There were no patches to be seen on the throat. The child was apparently quite convalescent and taking full diet with relish. The bacteriological cultivations from the throat showed a large number of streptococci and staphylococci, with a few well-defined diphtheritic bacilli. (Fig. 14.)

Diphtheria with pertussis.—Maud H——, aged five years, suffering from pertussis, on December 22, 1894, developed feverish symptoms with soreness of the throat. The pulse rose from 120 to 140, respiration from 20 to 40, and the temperature from normal to 104° F. There were vomiting and general malaise, and on examination of the throat it was found to be covered with diphtheritic membrane. The glands were enlarged, but there was no albumen in the urine. Ten cubic centimetres of No. 1 Behring's solution were injected, with the result that the temperature fell to normal in six hours and the feverish symptoms subsided, the child making a rapid and uninterrupted recovery. Bacteriological examination showed diphtheritic bacilli in large numbers, but few cocci. (Fig. 15.)

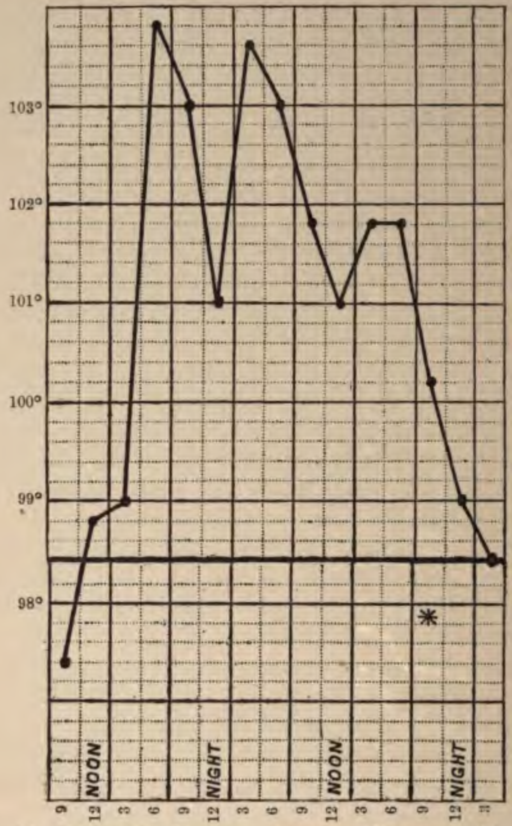

FIG. 15.—MAUD H., 5 YEARS. ADMITTED DECEMBER 22, 1894. ANTITOXIN INJECTED AT 10.15 P.M.*

In some cases it has been necessary to repeat the employment of antitoxin after a few hours—in fact, our rule has been to employ a second dose within twenty-four hours if the membrane has not shown marked signs of improvement. Sometimes we have found the membrane reform, but this has been comparatively rare, and the fresh patches have speedily detached. Although it has been stated that no constant or improved effect upon either the temperature or pulse rate is attributable to antitoxin, we have mostly found that the pulse improved somewhat in strength, and the temperature usually, but not always, fell. (Fig. 16.) The fall of temperature, however, may have had little reference to the treatment, since a fall often occurs with the development of membrane under other modes of treatment; but it may be worth noting that, contrary to some statements that have been made, we have certainly not found any material rise of temperature after the injection.

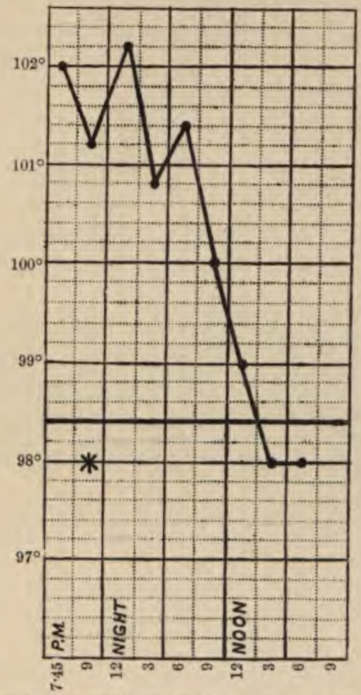

Fig. 16.—Henry B., aged 2 years 9 months. Admitted January 4, 1895. Antitoxin at 9.30 p.m. same night

Much has been said of ill results from the use of this remedy. A rash has been mentioned, and albuminuria is stated to be a frequent result.

Tonsils; soft palate; rash.—Charles B——, aged four years, was quite well and attending school the day before admission, but that same night complained of pain in the throat, vomited, and seemed generally feverish. When seen on the day of admission, December 24, 1894, the patient was a well-nourished child with marked dyspnœa and slight cyanosis, enlarged glands at the angle of the jaw, and some cellulitis of the neck. The tonsils were enlarged and covered with typical diphtheritic membrane, which also extended to the uvula and soft palate. There was no nasal discharge. The temperature was 101·6° F., the respiration was 20, and the pulse was 120, weak, and very compressible; the urine (sp. gr. 1015) contained no albumen, and no urates in excess. Ten cubic centimetres of No. 1 Behring's solution were injected deep into the muscles of the thigh, and three hours afterwards the temperature had fallen to normal, the respiration was 24, and the pulse 120, but fuller. The next morning the patient's dyspnœa had quite disappeared, and the

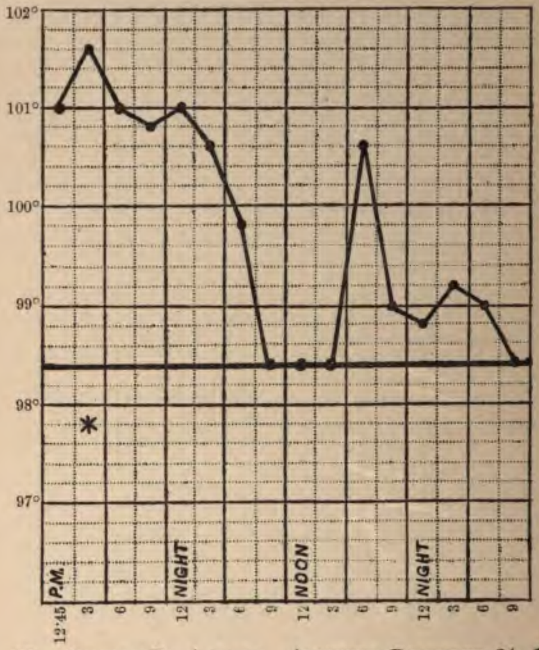

FIG. 17.—CHARLES B., 4 YEARS. ADMITTED DECEMBER 24, 1894. ANTITOXIN AT 3 P.M. SAME DAY

membrane was rapidly becoming detached from the throat; there were no bad symptoms. The following day an urticaria was noticed rapidly extending from the site of puncture over the body, but giving apparently no discomfort to the patient, whose general condition was excellent. Bacteriological examination showed a large number of diphtheritic bacilli. (Fig. 17.)

Diphtheria treated with antitoxin; rash.—Frederick D. M——, aged three years and nine months. Admitted December 7, 1894. A patch of whitish-grey membrane about the size of a threepenny-piece on left tonsil. Antitoxin given on admission. On the 15th profuse urticaria all over trunk and limbs, not irritable, gradually faded in an hour or so; pulse very weak for four or five days. Recovery.

Case treated with antitoxin and tracheotomy; intermittent pulse, and rash.—Alice B——, aged six years. Admitted November 17, 1895. On the 12th was sick and complained of her throat being sore. On the 14th she had croupy cough, which did not improve, and breathing became very short at night. On admission tonsils red; very thin exudation on the right tonsil; glands in right side of neck swollen and painful; breathing stridulous; some retraction of chest; cough croupy; voice whispering; very fretful; slight sickness; difficulty in swallowing; urine containing a trace of albumen. Was put into a steam tent, and two drachms of ipecacuanha wine given until sickness set in. 10 c.c. of antitoxin were injected, and later the breathing became more shallow and there was more depression of intercostals. Tracheotomy performed an hour and a half later; some membrane expectorated at the time of operation. On the 19th several small pieces of membrane coughed up. The child gradually improved from that date until on the 23rd the tracheotomy tube was removed. On the 24th a slight rash appeared and gained in brightness on the 26th, when the temperature was 99·6°. On

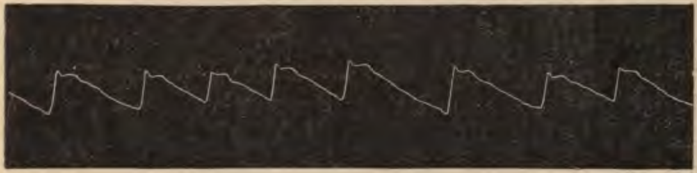

FIG. 18.—ALICE B., AGED 6 YEARS, FOURTEEN DAYS AFTER TRACHEOTOMY AND INJECTION OF ANTITOXIN FOR DIPHTHERIA

the 28th the rash disappeared ; the pulse then noticed to be weak and irregular, otherwise general condition satisfactory. Convalescence uninterrupted.

The rash generally resembles urticaria, and may last two or three days. It usually starts near the site of the injection, but mostly becomes diffused more or less over the whole of the trunk and extremities; sometimes it is more like a patchy erythema, and occasionally it may simulate the eruptions of measles or scarlatina. The appearance of the rash is frequently associated with a slight rise of temperature, which continues for some days. I have not seen any ill effect from these rashes, and they have not appeared to me to influence the convalescence in any way.

Then with regard to albuminuria, my own experience is that albuminuria is not rendered more frequent by the employment of antitoxin, although the statistics of the Metropolitan Asylums Board indicate an increase in the percentage of cases exhibiting this symptom. In 1894, 24·1 per cent. of the cases observed presented albuminuria, while in 1895, when antitoxin was used, albuminuria was present in 41·5 per cent. of the cases. This apparent increase in the number of cases of albuminuria may, however, be possibly explained by the larger number of survivors during the antitoxin year. Much stress has been laid by Mr. Lennox Browne upon the occurrence of albuminuria as the result of antitoxin, and he quotes numerous observers who accuse serum of directly provoking albuminuria, and he goes so far as to say that marked and increased albuminuria, especially if accompanied by diminished quantity of urine, should be accepted as contra-indicating a continuance of the injections. He also lays stress on the fact that six out of eight of his first cases died with anuria as the most prominent symptom, and while he hesitates to say that the serum will produce anuria in a patient who is not suffering from diphtheria, he maintains that it increases the well-known tendency to renal complications in those intoxicated with its specific poison. He quotes Hansemann in support of these views, and he mentions a case of a child who died of nephritis after injections of serum in whom it seemed 'quite indubitable that the nephritis was a result of the large doses of serum which the child had received.' These views are certainly at variance with the observations of those who have considerable clinical experience. In the recent Report to the American Pediatric Society, referring to their experience in private practice of the antitoxin treatment of diphtheria in over 5,000 cases, the observers concluded that there was little if any evidence to show that nephritis was caused in any case, that the number of cases of genuine nephritis which came under their observation was remarkably small, and of fatal cases there were only fifteen. While it must be admitted that the records of albuminuria have been more frequent since the introduction of antitoxin, it should be remembered that albuminuria rarely causes any symptoms in diphtheria, and it is probable that although the condition existed, it was not often looked upon as of any particular consequence. Since the introduction of antitoxin, however, this albuminuria has been quoted as one of the results of the new treatment, but it is perfectly possible that the condition is really not more common, although it has been more frequently reported. The figures published by the Metropolitan Asylums Board do not support the statement that antitoxin frequently leads to renal inflammation, and albuminuria, even if more frequent, may merely be the result of a greater number of cases surviving the initial stages of the disease.

Fauces and larynx (?) ; **antitoxin** ; **tracheotomy.**—William H. G——, aged two years. Admitted on August 4, 1896, with pneumonia, which progressed slowly but favourably for eight days, when the temperature fell to 99·2°. The urine contained albumen throughout the pneumonic attack. On the 13th about 10 P.M. signs of laryngeal obstruction developed ; the tonsils were inflamed and swollen, meeting in the middle line ; no membrane was seen. Hot fomentations gave a certain degree of relief. On the 14th dyspnœa was worse ; much sucking in ; lips blue ; pulse very weak. Tracheotomy was performed at 9.30 A.M. and antitoxin (10 c.c. Brit. Inst. Preventive Medicine) injected at same time ; throat swabbed out hourly with 1 in 1,000 perchloride of mercury ; several pieces of membrane were brought out on the sponge. The same day there was some regurgitation of fluids through the nose. Small traces of albumen continued during the next four days, but otherwise progress was favourable.

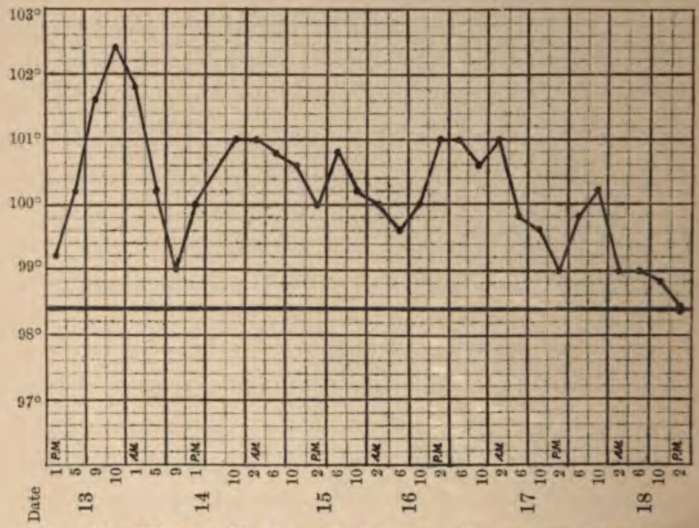

FIG. 19.—WILLIAM H. G., AGED 2 YEARS. DIPHTHERIA COMMENCED AUGUST 13, 1896. TRACHEOTOMY AND ANTITOXIN AT 9.30 A.M. ON AUGUST 14

Three points of special interest may be mentioned in connection with the above case :—

1. The case developed under observation, hence the initial rise of temperature was recorded, and it will be seen that it

just reached 102·4° and then fell before tracheotomy was performed.

2. The tracheotomy and antitoxin were followed by a slight rise of temperature, but the pulse became and continued remarkably steady, varying from 116 to 124.

3. The occurrence of albuminuria had been noted as a febrile symptom during the attack of pneumonia, and previous to the diphtheritic attack, hence the albuminuria cannot in this case be attributed to the use of antitoxin.

Some stress has been laid upon the production of pains in the joints similar to those of acute rheumatism since the introduction of the serum treatment, and these pains have been attributed to the serum. Mr. Lennox Browne states that in the pre-antitoxin days joint pains were practically unknown except—and this is an important exception—in cases of complex diphtheria of a malignant type, and he endeavours to discredit the views of some whom he calls 'laboratory workers,' who have asserted that the articular swellings are of no clinical importance. It may be worth pointing out that the cases of joint pains noted in the Metropolitan Asylums Board Report only amount to 4·7 per cent., and also that in the report on the 5,000 cases from the American Pediatric Society joint pains are not mentioned as complications. I may add that, dealing with smaller numbers at the Evelina Hospital, we have not seen any of these cases simulating articular rheumatism.

With regard to the time at which the treatment should be commenced, all statistics and all observers agree that the results obtained are infinitely better when the treatment is commenced early. After the third day the protective influence of antitoxin seems not to be very great, and the mortality when the treatment has been so far delayed does not differ materially from that obtained with the ordinary methods; but, on the other hand, if the cases come under observation during the first or second day and the treatment is commenced at once, the reduction of the mortality is considerable.

The Report of the American Pediatric Society gives results which are superior to those obtained by any other observers. Thus, while the Metropolitan Asylums Board found that the percentage of mortality between the ages of two and five was 33·5 per cent., for the same ages the American Society found a mortality of 14·7 per cent. Under two years of age their mortality was 23·3 per cent., as compared with 51·1 per cent. of the Metropolitan Asylums Board. These statistics are drawn from the private practice of 615 different physicians in widely separated localities, hence the possible influence of local conditions can be excluded, and the personal bias of individual members of the profession can also be eliminated.

In comparing the results obtained in private practice with those from hospital treatment, it must be remembered that the former undoubtedly include many milder cases, and that the children are generally better able to face the dangers of the later stages of the disease by being in a better state of nourishment and development.

The class of cases in which the improvement effected by antitoxin appears to be the most noteworthy are those in which the diphtheria affects the larynx. I have previously referred to the improvement in the results obtained from intubation since the introduction of antitoxin, and it is satisfactory to find that the American observers agree in stating that antitoxin checks the rapid spreading of the membrane downward in the respiratory tract, hence in the cases in which they have performed intubation they have obtained a mortality of 25·9 per cent. as against a previous mortality of 51·6 per cent. before the use of antitoxin. They have also found that over a half of the laryngeal cases do not require any operation at all, and this must undoubtedly be laid to the credit of antitoxin in checking the spread of the disease and favouring the detachment of membrane.

A similar improvement in cases of laryngeal stenosis has been noted by Zuppinger in his report upon 160 cases treated with antitoxin at the Crown Prince Rudolf Children's Hospital in Vienna. In twelve out of fifty-one cases the laryngeal stenosis improved, and operative interference was averted; while in the previous year forty-five out of forty-six laryngeal cases required operation.

It is somewhat doubtful whether the occurrence of various forms of diphtheritic paralysis is in any way influenced by the employment of antitoxin. The cases which have come under my observation since the employment of this treatment have been remarkably free from paralytic affections. Recently I have seen some paralysis of the soft palate and slight loss of power in the forearms in a nurse who had been treated with antitoxin; but, so far as children in the hospital are concerned, paralytic sequelæ have been absent from the records. We were able at one time to collect nearly all the cases which had been treated with antitoxin at the Evelina, some six months after they had left the hospital, and none of the children exhibited any paralytic affections at the time when they were examined, and, so far as the parents' accounts can be trusted, they had been free from any trouble since leaving the hospital. Still, the returns of the Metropolitan Asylums Board indicate that while 403 cases (13·2 per cent.) of diphtheritic paralysis occurred in 1894, 732 (20·7 per cent.) occurred during 1895, when antitoxin was being employed. The Report of the American Society states that trustworthy data could only be obtained in 3,384 cases, and of this number there were paralytic sequelæ in 328 cases, or 9·7 per cent. Of the 2,934 cases which recovered, paralysis was present in 276, or 9·4 per cent.; of the 450 cases which died, paralysis was noted in 52, or 11·4 per cent.

It must be remembered that statistics are frequently fallacious, and that in attempting to estimate the value of antitoxin, before satisfactory comparison can be made, we require to have some measure of the strength of the antitoxin employed. The different forms of serum supplied by different makers seem to vary considerably in efficacy, and when we consider that many practitioners have hesitated to use the dose recommended for adults, it will at once be seen that the statistical method is not satisfactory. Even the strength of the serum supplied from the same source has in many cases been altered; thus the serum supplied by Behring at the present time is considerably stronger than that which was originally introduced.

Mode of administration.—The serum can be injected in any place where the subcutaneous tissue is loose. Some have recommended that it should be injected into the buttock, others into the flank, but my own practice has been to inject sometimes into the subcutaneous tissues over the thigh, sometimes over the abdominal wall. The syringes employed must be of somewhat large size, and it is advisable that they should be able to be readily detached so that every portion may be disinfected by boiling. The syringe usually employed holds about 25 c.c., and the washer of the plunger is made of asbestos so that it can be tightened up when within the tube by means of a screw at the end of the piston rod. A piece of indiarubber tubing is sometimes employed to connect the needle with the nozzle of the barrel, and this has the advantage of permitting slight movement of the patient without additional pain. If the operation is performed with care, the use of this indiarubber tubing is not necessary. It is only when the serum is rapidly injected that patients experience any pain beyond that produced by the prick of the needle. Before using the serum it is advisable to wash the skin thoroughly, first with soap and water, and then with a solution of carbolic acid; and after the injection has been completed, firm pressure should be made over the site of the injection for a few minutes so as to retain the serum as far as possible. Sometimes a small pad of sublimate wool has been placed over the site of the puncture, and this, if the serum exudes, forms a protective covering. After the injection some degree of local swelling is formed, but this disappears in the course of an hour or so. When ordinary simple and aseptic precautions are taken, we have not seen any local inflammation.

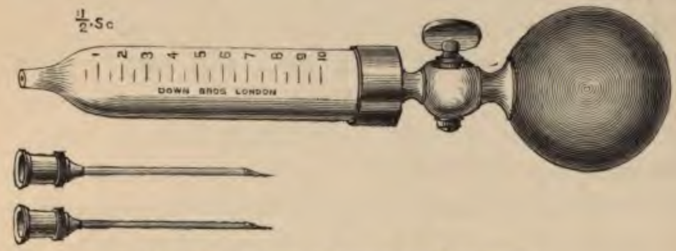

FIG. 20.—KOCH'S SYRINGE FOR ANTITOXIN

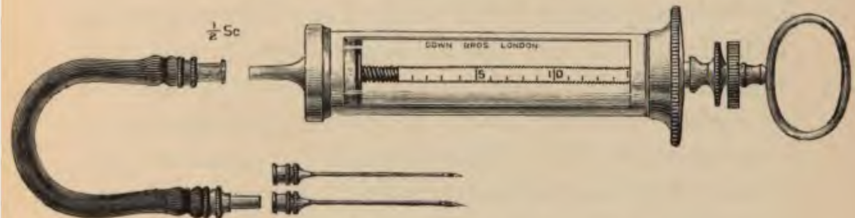

FIG. 21.—ROUX'S SYRINGE FOR ANTITOXIN

Dosage.—It is most important to remember that the dose of serum to be employed does not depend upon the age of the patient but upon the urgency of the symptoms, and that these are almost always more severe in young children. A second point, which follows as a corollary to the first, is that the dose depends to some extent upon the date of the disease when the patient first comes under observation. In hospital practice doubtless the tendency has been to employ relatively large doses owing to the delay which commonly occurs before the children are brought to the hospital. In broad terms it may be said that it is always better to begin with a fairly large dose, and to employ a smaller dose later if necessary. As above indicated, the amount given must also vary with the potency of the serum employed. Much disappointment has arisen from attempts to compare results obtained with different preparations which vary in strength, and much of the doubt which has been expressed as to the value of the treatment has probably arisen from an attempt to regulate the dose according to the age of the patient. It is also probable that disappointing results have followed from the disinclination to use the seemingly large bulk of fluid recommended in the earlier days of the introduction of antitoxin. There is no doubt a prejudice in favour of the smaller doses by the hypodermic method of administration. Practitioners have been so much in the habit of employing hypodermic doses of from one to five minims, that the dose of 10 or even 20 c.c. is regarded with feelings akin to dismay. These doses are no longer necessary, though they were frequently employed when the serum was first introduced. With improved methods of preparation it has been found possible to produce serum of greater potency, and it has also been found possible to express the degree of potency in terms of immunising power without reference to the absolute volume of serum; that is to say, that the strength of the serum is expressed in terms of its protective value upon guinea-pigs injected with such a dose of toxin as to be fatal in twenty-four or thirty-six hours to a control animal. The Report to the American Pediatric Society recommends that for a child over two years old the dose should be in all laryngeal cases with stenosis and in all severe cases 1,500 to 2,000 units for the first injection, to be repeated in from eighteen to twenty-four hours if there be no improvement, a third dose being given, if necessary, after a similar interval. For severe cases in children under two years, and for mild cases over that age, the first dose should be 1,000 units, repeated if necessary. The Medical Superintendents of the Metropolitan Asylums Board consider that the best results may be obtained by giving a dose of 1,000 Behring's immunisation units every twelve hours for the first twenty-four, thirty-six, or forty-eight hours, according to the gravity of the case; and if necessary, a subsequent injection of half the amount daily for such time as the exudation may remain adherent. In our work at the Evelina we have found that it is only in exceptional cases that such frequent doses are required. In the majority of our cases a single dose has been sufficient, and we always begin with a dose corresponding to 1,000 units of immunity. We repeat the dose however, according to circumstances, either twice or three times, commonly at intervals of twenty-four hours.

Conclusion.—I cannot conclude without indicating that my own experience of the value of antitoxin, corroborated by the statistics from larger numbers than can possibly fall within the individual experience of one physician, has rendered me very sanguine about the future in store for this treatment. I commenced employing it with a certain degree of adverse bias, due possibly to the recent failure of Koch's serum to justify the high expectations with which it was greeted; but as I witnessed the results obtained by antitoxic serum in diphtheria, I became more and more convinced of its efficacy if employed sufficiently early. Whereas a few years ago a large number of cases of diphtheria, especially those affecting the larynx, or naso-pharynx, were regarded as extremely hopeless, I now feel that the whole prognosis depends more on the time at which the case can be treated than upon the site attacked. Antitoxin has produced no ill results of any importance, while, in the opinion of numerous competent observers, it has been the means of saving life in many apparently hopeless cases. Without for one moment underrating the value of bacteriological research, and the interest attaching to the proof of the existence of Loeffler's specific bacillus, I would urge the early employment of antitoxin in all cases in which the clinical features of diphtheria are present, without delaying while cultivations are made to prove the diagnosis. In fact, I believe that by the early recognition of the disease, and by the use of antitoxin at an early stage, we shall in the future be able to reduce very materially the death-rate from diphtheria.

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